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CHEMISTRY IN SPACE

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CHEMISTRY IN SPACE

FROM

PROFESSOR J. H. VAN 'T HOFF'S

'DIX ANNÉES DANS L'HISTOIRE D'UNE THÉORIE'

TRANSLATED AND EDITED

BY

J. E. MARSH, B.A.

DEMONSTRATOR IN ORGANIC CHEMISTRY AT THE UNIVERSITY LABORATORY
OXFORD

Oxford

AT THE CLARENDON PRESS

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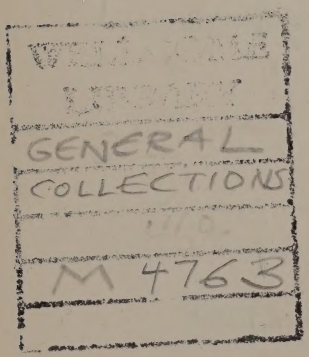

PREFACE.

THE almost universal adoption of the hypothesis of the tetrahedral carbon atom renders it unnecessary to put forward any excuse for offering Professor Van 't Hoff's work to English students of Chemistry. But a word or two is perhaps necessary to assist them in reading it. In the first place, from the numerous references to original papers it will be obvious that a vast amount of literature has been condensed into a very small space. Thus it happens that many compounds of importance are merely mentioned without any adequate description of them as to their relationships, properties and transformations. The student should therefore consult frequently a good work of reference or, better still, if possible, the original memoirs.

It will also be of advantage, for those to whom the subject is new, to leave the first chapter till the end. The first chapter contains a translation of the earliest memoirs on the subject, and the ideas are incompletely developed, obscure, and sometimes erroneous.

One word finally as to a matter of a practical kind: it will be found to be of the greatest importance to construct or procure models of tetrahedrons in order to illustrate the position of the groups about one or more

carbon atoms, and especially in the case of closed chain compounds to represent every carbon atom in the formula in this way.

The present work is a considerable extension of the French edition; and it is only just that I should state that whatever merit it may possess in that respect is chiefly due to the invaluable assistance and advice which I have received from the Author.

J. E. M.

January, 1891.

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CHEMISTRY IN SPACE.

HISTORICAL.

ORIGINAL ENUNCIATION OF THE THEORY.

THE theory of what is known as 'the asymmetric carbon atom' originated simultaneously in France and Holland, and was enunciated independently by two chemists, and we think it desirable to quote the chief part of the text of the two original memoirs as they were given by their authors.

In the Bulletin of the Chemical Society of Paris, November, 1874, p. 337, J. A. Le Bel expressed his conceptions in the following manner:—

'*On the relations which exist between the atomic formulae of organic bodies and the rotatory power of their solutions.*

'We have hitherto possessed no certain rule which allows us to predict whether or not the solution of a substance should manifest rotatory power (in respect of polarised light). It was simply known that the derivatives of an active substance were in general also active; but it was often observed that rotatory power might disappear in certain derivatives, and even in the more immediate derivatives, while it was preserved in derivatives much more remote. Starting from considerations of a purely geometrical character I have arrived at the expression of a more general law. Before giving the

reasoning by which I have arrived at this law, I propose to give the data on which it is founded, and finally to discuss the verifications furnished by the present state of our chemical knowledge.

'The researches of Pasteur and others have completely established the correlation existing between molecular dissymmetry and rotatory power. If the dissymmetry only exists in the crystalline molecule the crystal alone will be active; if, on the other hand, it belongs to the chemical molecule, rotatory power will be manifested in solution often, and also by the crystal, if the structure admits of its perception, as is the case with sulphate of strychnine and the alum of amylamine. There are, moreover, mathematical proofs of the necessary existence of this correlation, which we may consider an absolutely ascertained fact.

'In the reasoning which follows we shall not take into account the dissymmetries which might result from a possible orientation possessed by the atoms and monatomic radicals in space; as a consequence of considering them equivalent to spheres or material points, equal if the atoms or the radicals are equal, and different if they are different. This restriction is justified by the fact that without recourse to such orientation it has become possible to account for all the cases of isomerism hitherto observed, and the discussion at the close of this memoir will show that the appearance of rotatory power can be equally well predicted without recourse to the hypothesis just mentioned.

'*First general principle.*—Let us consider a molecule of a chemical compound having the formula MA_4: M being a simple or complex radical combined with four atoms A, capable of replacement by substitution. Let us replace three of them by simple or complex monatomic

radicals different from A[1] and also from each other; the body obtained will be unsymmetrical. In other words, the group of radicals RR′R″A if considered as material points, being each different, forms by itself a structure not superposable on its image reflected in a mirror, and the residue M cannot re-establish symmetry. In general, therefore, we may assert that when a body is derived from the original type MA_4 by the substitution of three atoms A by three new atoms or radicals of different kinds its molecule will be unsymmetrical, and it will exhibit rotatory power.

'But there are two exceptional cases distinct in character.

'(1) If the molecular type has a plane of symmetry containing the four atoms A, the substitution of these by radicals (which we must consider as not capable of orientation) can in no way alter the symmetry in respect of this plane, and in such instances the whole series of substitution products will be inactive.

'(2) The last radical replacing A may consist of the same atoms as all the rest of the group into which it enters, and these two equal groupings may have on polarised light either a neutralising effect, or an effect of increased activity: if the former is the case, the body will be inactive. Now it is possible that this arrangement may be met with in the case of a derivative of an active unsymmetrical body where there is but little difference in constitution, and we shall see later a remarkable instance of this.

'*Second general principle.*—If in the fundamental type we substitute only two radicals R, R′, there may be symmetry or not according to the constitution of the primitive type MA_4. If this molecule had originally

[1] The original has 'M.'

a plane of symmetry passing through the two atoms of A which have been replaced by R and R′, this plane will remain a plane of symmetry after the substitution; and the body obtained will be inactive. From our knowledge of the constitution of certain simple types we are able to assert that certain bodies derived from them by two replacements will be inactive.

'Again, if it happens not only that a single substitution furnishes only one derivative, but also that two and even three substitutions only furnish one and the same chemical isomer, we are obliged to admit that the four atoms A occupy the angles of a regular tetrahedron, whose planes of symmetry are identical with those of the whole molecule MA_4; in this case also no bisubstituted body can have rotatory power.

'*Application to saturated bodies of the fatty series.*—All the saturated bodies of the fatty series are derived from marsh gas CH_4 by replacement of the hydrogen by different radicals. Provided that the atoms of hydrogen are not in the same plane, a supposition on which the very existence of active trisubstituted bodies is based, we can apply the first general principle and assert that the substitution of three different radicals will furnish active bodies, and whenever in the constitutional or typical formula of a substance we meet with one carbon atom combined with three monatomic radicals different from each other and from hydrogen, we ought to find it an active body.

'Further, as marsh gas never furnishes more than one derivative by two substitutions [1], we can apply the second general principle and assert that such derivatives are never active. Hence whenever we meet with a carbon atom combined with two atoms of hydrogen or with two

[1] 'Par deux et *par trois substitutions.*'

identical radicals, such a body ought not to manifest rotatory power. Let us now review the active bodies of the fatty series (as such are instanced the lactic, malic, tartaric, and amylic groups, and the group of sugars).

'*Fatty bodies with two free atomicities.*—We have not yet taken into account active unsaturated bodies, for we do not include in this class bodies obtained by the substitution of an active radical in an unsaturated inactive body, such as, for example, valerate of allyl.

'We have only to examine the case where the double linking of the unsaturated body is due to the disappearance of some of the radicals, the unsymmetrical grouping of which caused rotatory power in the corresponding saturated body. Since all the bodies with two free atomicities are derived from ethylene, it is to this latter we must, if possible, apply the general principles which we have previously employed.

'We shall neglect the case where the four atoms of hydrogen may not have determinate positions one to another, for it is clear that their replacement could not furnish unsymmetrical bodies. If, on the contrary, these relative positions are fixed, we can apply to ethylene the same reasoning as to marsh gas.

'If the four atoms of hydrogen lie in the same plane, which is a possible case of equilibrium, there will be no trisubstituted active derivative; nevertheless, we do not know examples of well-studied bodies derived from ethylene by three different substitutions, and we are therefore unable to solve this question at present.

'As to the second general principle, it is not applicable to ethylene, for the formula $CH_2=CH_2$ shows that by two substitutions chemically different isomers are obtained. This is not opposed to the possibility of the atoms being in the same plane, in which case the derivatives

by two substitutions will be inactive. In any other case, to explain the isomerism of the ethylene derivatives, we must suppose the hydrogen atoms placed at the angles of a hemihedral quadratic pyramid superposable on its image $\frac{P}{2}$, and we should obtain by two substitutions two isomers, one of which would be symmetrical, and the other unsymmetrical. These isomers will be both symmetrical if the two substituted radicals are the same, as is the case with maleic and fumaric acids. It will suffice, therefore, to study the optical character of two disubstituted derivatives, such as the amylene of active amyl alcohol $CH_2=C=\frac{CH_3}{C_2H_5}$, and its isomer $CH_3-CH=CH-C_2H_3$, to decide whether the four atoms of hydrogen are or are not in the same plane.

'*Aromatic Series.*—All chemists agree in considering that the atoms of hydrogen in benzene occupy fixed positions, we cannot then consider, as we did in the case of saturated bodies, a part of the molecule of benzene as a single material point; but this restrictive hypothesis will still hold in the case of the radicals or groups which replace hydrogen in benzene. The geometrical hypotheses which account for the isomerism of the aromatic series have already been discussed elsewhere; they assume that the atoms of hydrogen are situated at the six equal angles of a rhombohedron or at those of a right prism[1] on an equilateral triangular base. A simple geometrical reasoning shows that in either arrangement by two different substitutions there are obtained one unsymmetrical and two different symmetrical isomers; the existence of an active cymene which has been announced confirms these hypotheses which we will not discuss further.

[1] 'pyramide.'

'Without ascribing to the atoms of hydrogen in benzene any particular grouping, we can apply the first general principle to any three atoms of hydrogen whatever, provided they do not occupy a plane of symmetry of the whole molecule.

'Hence it follows that we shall discover active bodies whenever three atoms of hydrogen at least are replaced by different radicals. We find this inference realised in a large number of bodies of the camphor series.

'The case is not the same for spirit of turpentine; we know that this is derived, as also the camphor series, from paracymene, in which the radicals methyl and propyl occupy the positions 1 and 4 in Kekulé's hexagon, and as this is a plane of symmetry of benzene we have the reason why cymene is inactive. Now spirit of turpentine is derived from cymene by the substitution of two H_2 groups for two atoms of hydrogen; if these occupy the positions 2 and 6 or 3 and 5, symmetrical with regard to the plane of symmetry passing through 1 and 4, we shall have inactive isomers; on the other hand we shall have active isomers (terebenthene and camphene) if they occupy positions not symmetrical one to another, as 2 and 5 or 2 and 3; and one might apply the same reasoning to the other isomers of terebenthene.

'We see what amount of interest is attached to the study of active aromatic compounds, and how necessary it is that chemists who are dealing with bi- and tri-substituted derivatives of benzene capable of being active should attempt the separation of their dextro- and laevo-rotatory isomers. We will proceed to show that the bodies obtained by synthesis consist in fact of equal proportions of these isomers.

'*Theorem.*—When an unsymmetrical body is formed in a reaction where there are present originally only symme-

trical bodies, there will be formed in equal quantities two isomers of inverse symmetry.

'This is not necessarily true for unsymmetrical compounds formed in presence of active bodies themselves, or traversed by circularly polarised light, or, in short, submitted to some cause which is favourable to the formation of one of the unsymmetrical isomers. Such conditions are exceptional; and generally in the case of bodies synthetically prepared those which are active must necessarily be overlooked unless the chemist takes pains to separate the mixed isomeric products of which the combined action on polarised light is neutral. We have a striking example of this in the case of tartaric acid, for neither the dextro nor the laevo acid has ever been obtained directly by synthesis, but always the inactive acid or racemic acid which is a combination of equal parts of dextro and laevo acid.'

In a Dutch pamphlet, published in September, 1874, I expressed my own opinions as follows:—

'*A treatise on a system of atomic formulae in three dimensions and on the relation between rotatory power and chemical constitution.*

'I propose to offer certain ideas in a preliminary note in order to profit by the discussion which may follow.

'The atomic formulae at present in use are incapable of interpreting certain instances of isomerism: this defect which is becoming more and more evident is due perhaps to the absence of precise conceptions as to the relative positions of the atoms.

'Dealing in the first instance with organic bodies, if we suppose that the four affinities of carbon act in the same plane and in directions perpendicular to each other, the number of isomers derivable from methane

CH_4 is as follows: none in the cases CH_3R and $CH(R)_3$; two in the cases $CH_2(R)_2$, CH_2RR_1 and $CHR_2(R)_2$; and three in the cases $CHR_1R_2R_3$ and $CR_1R_2R_3R_4$; this number is evidently larger than we are as a matter of fact acquainted with.

'On the other hand, if we grant that the affinities of the carbon atom are directed towards the angles of a regular tetrahedron, of which this atom occupies the centre, there results a marked coincidence between the theory and the facts. According to this hypothesis the number of isomers becomes as follows:—

'No isomers in the cases CH_3R_1, $CH_2(R_1)_2$, $CH_2R_1R_2$ and $CHR_2(R)_2$; the case alone $CHR_1R_2R_3$, or more generally $CR_1R_2R_3R_4$, allows the prediction of isomerism; in other words,—If the four affinities of the carbon atom are saturated by four different groups, we obtain two tetrahedrons of which one is the nonsuperposable image of the other, that is to say, we have to deal with two different structural formulae in space. Consequently according to this hypothesis the compounds $CR_1R_2R_3R_4$ possess a different character from that of the compounds $C(R_1)_2R_2R_3$, $C(R_1)_3R_2$ or $C(R_1)_4$, a difference which is not explained by atomic formulae in their present form.

'In offering this first conclusion it appears to me possible to show that the compounds containing an atom of carbon combined with four different groups, which I will call an "asymmetric" atom, are in a special manner characterised as much by the fact of isomerism as by their peculiar properties. This fact offers a serious obstacle to the application of the constitutional formulae hitherto employed.

'First Part.—I. *Relation between the asymmetric carbon atom and rotatory power.*

'(*a*) Every carbon compound which in solution rotates

the plane of polarised light contains an asymmetric carbon atom.

'To justify this statement it is only necessary to pass in review the active bodies of ascertained constitution (as such may be quoted the lactic, tartaric, camphoric groups, and the group of sugars).

'(*b*) The derivatives of optically active bodies lose their rotatory power if the asymmetry of the carbon atom disappears. This in general does not take place otherwise. (The examples quoted apply here.)

'(*c*) On reviewing the compounds which contain an asymmetric carbon atom, it is clear that proposition (*a*) can not be taken in a converse sense, that is to say, that a compound of such a nature acts necessarily on polarised light; we can explain this by the following considerations:—

'(1) The compounds in question may be composed of an inactive mixture of two oppositely active isomers.

'(2) The rotatory power may have escaped notice owing to its feebleness or the want of solubility of the compound.

'(3) The presence of an asymmetric carbon atom may of itself be an insufficient condition, and not only the difference of the groups, but also their nature should be taken into consideration.

'However that may be, the above observations show that a relation may exist between atomic constitution and rotatory power, which may serve in default of better arguments to explain the following cases:—

'(1) Active amyl alcohol,

$(CH_3)(C_2H_5)CH.CH_2OH$,

'(2) Inactive citric acid,

$(CH_2CO_2H)_2COH.CO_2H$.

'(3) Most simple active compounds,

the alcohol $CH_3CH.OH\,C_2H_5$,

the acid $CH_3CH(CO_2H)C_2H_5$,
diatomic alcohol $CH_3CH.OHCH_2OH$,
the hydrocarbon $CH_3C_2H_5CHC_3H_7$,
the aromatic hydrocarbon $CH_3C_2H_5CHC_6H_5$.

'(4) Prediction of inactive series,
hydrocarbons of the normal series $CH_3(CH_2)_4CH_3$.
Primary alcohols and the corresponding acids derived from the normal hydrocarbons.

'(5) Prediction of the possibility of separating the body CHBrClI into two isomers oppositely active.

'II. *Relation between the asymmetric carbon atom and the number of isomers.*

'Possibly the presence of asymmetric carbon is insufficient of itself to produce rotatory power; yet its presence must, according to the hypothesis proposed, lead to an isomerism manifesting itself in some way or other, an isomerism which can predict double the number of bodies foreseen by the use of present formulae if it deals with one asymmetric atom, and many more in the case of several such atoms. In fact, it appears possible to point out compounds exhibiting the apparent anomaly in question, which Wislicenus has called geometrical isomerism, insisting on the evident insufficiency of existing hypotheses, though without offering a more satisfactory explanation.

'(As applicable examples may be instanced dibrom- and isodibrom-succinic acids, citra-, ita- and mesabromopyrotartaric, and citra-, ita- and mesamalic acids.)

'Second Part.—I have hitherto dealt with the application of this hypothesis to saturated bodies (excepting always certain benzene derivatives); for the sake of completeness it is necessary to deal with:—

'*The influence of the new conception on the series of unsaturated bodies having two free atomicities.*

'To represent the double bond between two carbon atoms, we suppose two tetrahedrons having one of their edges common, so that the four groups R_1, R_2, R_3, R_4 combined respectively to the two atoms of carbon occupy the free angles, and are situated in one plane.

'If all the groups R_1, R_2, R_3, R_4 are identical, or if there is equality only between R_1 and R_2, R_3 and R_4, there will be only one relative position possible; if, on the other hand, R_1 and R_2 are different, and at the same time R_3 and R_4, no matter whether the groups R_1 and R_3, or R_2 and R_4 are identical or not, there will be two different relative positions enabling us to predict a case of isomerism not interpretable by the aid of the ordinary atomic formulae.

'From a study of the subject it seems that the following compounds are instances of this isomerism (as such are given, fumaric and maleic acids, bromo- and isobromomaleic, citra- ita- and mesaconic, crotonic and isocrotonic, chloro- and isochlorocrotonic acids).

'Third Part.—It only remains to consider compounds having a triple bond between the carbon atoms, for example, acetylene. Such compounds may be represented by two tetrahedrons which have three angles in common, the groups combined with the two carbon atoms occupying the free angles. It is clear that in this case the hypothesis entails no considerations other than follow from the formulae in use.

'Finally, I think I am entitled to observe that:—

'(1) The new hypothesis leaves no phenomenon unexplained that the theories in use are capable of interpreting.

'(2) Certain properties and certain isomerisms hitherto unexplained are explicable by the new hypothesis.

'(3) The observation as to bodies which in solution are optically active has some analogy with that of

Rammelsberg in the case of active crystals. This scientist, starting from the researches of Herschell and Pasteur, asserts that the property of rotating the ray of polarised light in the solid state is accompanied by the existence of two crystalline forms, each the non-superposable image of the other. It is plain that we are here dealing with a relative position of molecules in the active crystal perfectly analogous to that of the atomic groupings in the active molecule, a position which entails the absence of a plane of symmetry in the active crystals mentioned by Rammelsberg, and also in the tetrahedrons representing, according to my hypothesis, the molecules endowed with rotatory power.'

My pamphlet, 'La Chimie dans l'Espace,' appeared in May, 1875, and its German translation by Hermann, 'Die Lagerung der Atome im Raume' (1877), called forth two extremely opposite criticisms from two chemists of the first rank.

The favourable criticism of Wislicenus was inserted by him as a preface to the translation mentioned; it was expressed in the following terms:—

'It is no long time since strong protests were frequently made by the champions of the most advanced views in theoretical chemistry, against the idea that chemistry could ever reach such a point as to bring forward the conception of the position of the atoms in space in order to explain the properties of a compound.

'Such objections were due to a wide-spread obstinate misunderstanding of the conception of so-called structural chemistry, and were justified by the empirical condition of the facts at that time and in the condition also of the questions which engrossed especially the interest of research.

'It was even then, however, a matter of specu-

lation that the elementary atoms composing a molecule, so far as they could be reckoned with at all, must be in some way or other distributed in space, and that the same atoms having the same order of combination in complicated molecules may still be differently arranged in space, and that in this way possibly explanation may be found for slight differences in the properties of molecules identical in structure. Nay, there even existed isolated facts which demanded some attempt at explanation in this direction. Such ideas, to be sure, were either not at all or very diffidently and indefinitely expressed.

'In the meantime the study of isomeric organic compounds, which especially characterises the present position of chemical science, continued its natural course and led to indisputable facts, for the understanding of which the structural theory gave no further help.

'My work on paralactic acid obliged me to express the opinion that the facts compelled me to explain the difference between isomeric molecules having the same structural formulae by the different position of their atoms in space. Hence I openly entered the field for the rectification of chemical science by introducing geometrical conceptions into the doctrine of the constitution of molecules.

'We are indebted to Van 't Hoff for his having performed this service in a perfectly definite and in the happiest manner. The fundamental conception of his theory lies in the consideration that the compounds of a carbon atom with four different simple or compound radicals must afford two cases of isomerism.

'Striking as this thought appeared on reading Van 't Hoff's pamphlet, "La Chimie dans l'Espace," it was also engrossing for me in its further mathematical develop-

ment, and its application to the constantly increasing number of cases of what I have called geometrical isomerism and to optically active organic substances.

'It may be that the consequences of Van 't Hoff's theory go beyond our present requirements, and that some of its special applications may in time not receive complete confirmation. Yet the theory of carbon compounds has taken a real and an important step forwards, and this step is in a new direction and thoroughly necessary. The considerations most firmly based heretofore are developed in a consecutive logical manner and supported, and at the same time the theory extends to actually observed cases which appeared to lie outside its sphere.'

Kolbe's criticism[1], of an entirely opposite character, merits comparison. He says:—

'In a paper published lately under the same title, I have ascribed as one of the causes of the present decay of chemical research in Germany the lack of general and at the same time thorough chemical training, since no small fraction of our chemical professors are working to the great detriment of the science. In consequence of this, a miserable speculative philosophy, useless in reality, while apparently deep and ingenious, is springing up like a rank growth. Fifty years ago this was swept away and its place taken by exact scientific research. At the present time, however, it is again being rescued from the lumber-room of man's erratic speculations, by certain pseudo-philosophers seeking to thrust it forward surreptitiously, like some fashionably and gorgeously attired female, intruding into good society which is not her place.

'If any one supposes that I exaggerate this evil,

[1] Zeichen der Zeit, II. Journal für Prakt. Chemie, xv. 473.

I recommend him to read, if he has the patience, the recent fanciful publication of Messrs. Van 't Hoff and Hermann on "Die Lagerung der Atome im Raume." This paper, like many others, I should have been content to ignore had not a distinguished chemist taken it under his protection and warmly recommended it as a performance of merit.

'A Dr. J. H. Van 't Hoff, of the Veterinary College, Utrecht, appears to have no taste for exact chemical research. He finds it a less arduous task to mount his Pegasus (evidently borrowed from the Veterinary College) and to soar to his Chemical Parnassus, there to reveal in his "La Chimie dans l'Espace" how he finds the atoms situated in the world's space.

'His hallucinations met with but little encouragement from the prosaic chemical public. Dr. F. Hermann, assistant at the Agricultural Institute of Heidelberg, therefore undertook to give them further publicity by means of a German edition, which bears the title "Die Lagerung der Atome im Raume."

'It is not possible, even cursorily, to criticise this paper, since its fanciful nonsense carefully avoids any basis of fact, and is quite unintelligible to the calm investigator. To obtain, however, some idea of what may have been in the minds of the authors, it will suffice to read the two following paragraphs. The pamphlet begins with the words :—

'"Our modern chemical theory has two weak points. It does not express itself either as to the relative position of the atoms in the molecule or as to their methods of movement."

'The second paragraph at the top of page 35 in the memoir runs as follows :—

'"In the asymmetric carbon atom we have a medium

distinguished by the screw-like arrangement (sic) of its smallest parts, the atoms!"

'In view of the objection that it is unfair to quote isolated passages without giving the context, I can only refer to the memoir itself. Anybody can then satisfy himself that these passages with the context or without are equally absurd and unintelligible.

'It is characteristic of the present time with its poverty in and hatred for criticism, that two chemists almost unknown, one from a veterinary college and the other from an agricultural institute, should on the deepest and possibly insoluble problems of chemistry, especially the question of the position of the atoms in space, give their opinions with an amount of assurance and undertake the solution of these questions with an amount of audacity such as to astound the true investigator.

'I should, as I have said, have taken no notice of this matter, had not Wislicenus oddly enough prefaced the pamphlet, and not by way of a joke but in all seriousness warmly recommended it as a serviceable performance, on which account many a young inexperienced chemist might be led astray and set some store by these baseless and superficial speculations.

'Wislicenus delivers himself in his preface as follows:—

'"I was obliged to express the opinion that the facts compelled me to explain the difference between isomeric molecules of the same structural formulae by the different position of their atoms in space."

'It is one of the signs of the times that modern chemists hold themselves bound and consider themselves in a position to give an explanation for everything, and when their knowledge fails them to make use of supernatural explanations. Such a treatment of scientific subjects, not many degrees removed from a belief in

witches and from spirit-rapping, even Wislicenus considers permissible. He thus continues—

'"We are indebted to Van 't Hoff for his having performed this service in a perfectly definite and in the happiest manner," &c.

'Herewith Wislicenus makes it clear that he has gone over from the camp of the true investigators to that of the speculative philosophers of ominous memory, who are separated by only a thin "medium" from Spiritualism.'

Such was the début of this theory. Only fourteen years have passed, Kolbe is now dead, and, as if by the irony of fate his place at the University of Leipzig has been taken by Wislicenus.

Without entering into details as to the arguments brought forward since then on either side, it will be well to sum up in a few remarks the fortunes of the theory in order to examine it rightly to-day.

Restricting myself to facts I may state that no observation that has stood the test of experience has vitiated the truth of the theory; on the other hand, a large number of predictions permitted by the theory have been verified, as we shall see in the sequel. Add to this that Le Bel, whose researches have largely contributed to this result, was rewarded by the French Academy in 1881 with the Jecker Prize.

One proof among others that these verifications have resulted in gaining a considerable amount of support appears from two opinions recently expressed, one by v. Baeyer, and the other by Landolt, which I should like to quote here.

Von Baeyer[1], enumerating the properties of Carbon, writes on this subject in the third and fourth paragraph as follows:

[1] Ber. deutsch. Chem. Ges. 1885, 2277.

'III. The four valencies are equally distributed in space and correspond to the angles of a regular tetrahedron inscribed in a sphere.

'IV. The atoms or groups attached to the four valencies cannot change places with one another without a further reaction. Proof: there are two tetrasubstituted derivatives of Methane *a b c d*; Le Bel and Van 't Hoff's law.'

He adds, '*to these almost universally accepted propositions* I would now add the following.'

Landolt[1] writes on the subject of a retractive note as to the rotatory power of picoline:

'Hesekiel raises the question that in this case we appear to have an exception to Van 't Hoff's hypothesis, since Picoline contains no asymmetric carbon atom. In fact, this observation would be of the greatest interest, *since no single case is known at present at variance with this hypothesis.*'

A more conclusive sign of approval still, it appears to me, is to be found in the fact that the theory in question now forms part of elementary chemical teaching, and is to be found enunciated in the most widely used text-books, such as those of Von Richter, Roscoe and Schorlemmer, Von Miller, Pinner, Gorup-Besanez, &c. Finally there appears to be an evident tendency latterly to advance in the same direction; I mention in this connection the paper of v. Baeyer previously referred to, and a pamphlet by Wunderlich (Configuration Organischer Moleküle, Würzburg, 1886). To these may be added the opinion of V. Meyer (Ber. xxi. 784), and especially the remarkable work by Wislicenus (Abh. der kön. sächs. Ges. 1887), to which we shall have occasion frequently to refer.

[1] L. c. 1886, 157.

FIRST PART.

THE ASYMMETRIC CARBON ATOM.

I. Enunciation of the Fundamental Idea.

Insufficiency of the Atomic Conception.—The theory which is about to be developed proposes to solve to a certain extent, and for Carbon Compounds only, the problem as to the position of the atoms in the molecule. It offers itself as a perfectly natural development as soon as by the acceptance of the atomic and molecular conceptions the possibility has been recognised of a revelation by means of human research of the intimate nature of matter. It is necessarily a step into the region of hypothesis, but in a direction in which several theories have already been crowned with so much success that the conceptions gained still occupy a leading position in the whole domain of Chemistry. There is, for example, the molecular conception, with that which pertains to it, namely the determination of the relative weights of the molecules of different bodies according to Avogadro. There is also the atomic conception of Dalton, and the determination of the number and nature of the atoms which each molecule contains; and there are, finally,

speculations as to the manner in which those atoms are combined one with another in the molecule of which they are the components—speculations, in a word, as to molecular structure ; and from this point to the problem of the relative position of these atoms is only a step [1].

It is evident that arguments of this class, repellent from their inevitably hypothetical nature, have to sustain a protracted opposition; at the same time it can be said that at the present moment this opposition has disappeared in Germany with the death of Kolbe, and is now only sustained in France in the person of Berthelot.

The origin of the ideas which are to be developed has been that of every hypothesis, namely the impossibility of explaining certain phenomena by the aid of existing theories. It was proposed to deal with certain cases of isomerism inexplicable according to the current notions of molecular structure; although some of these cases, for example that of the tartaric acids, were already of long standing, yet the theoretical importance of the phenomena lay buried hidden by the use of terms such as 'Physical isomerism [2].' Wislicenus, however, took a different line on his discovery of an analogous phenomenon in the case of the lactic acids. This chemist recognised frankly the insufficiency of existing ideas in terms which I think right to mention [3], because they caused me to reflect on the problem in question :

'Facts compelled me to explain the difference between

[1] Attempts in this direction have been made some time since ; as an example may be mentioned Gaudin's 'L'Architecture du monde,' which appeared in 1873. It was only necessary to bring the ideas thus introduced into the region of fact.

[2] I enumerated at the time forty-three cases of this order. Maandblad voor Natuurwetenschappen, vi. No. 3.

[3] Wislicenus, Ann. Chem. Pharm. clxvi. 3 ; clxvii. 302, 346.

isomeric molecules of the same structural formulae by the different position of their atoms in space.'

The right of existence, or rather the necessity for the enunciation of opinions of the character of those now to be elucidated had thus been recognised by a chemist of the highest authority.

Introduction of the New Conception.—Difference was at that time recognisable between substances which nevertheless were formed of identical molecules according to the prevalent ideas: we have in both cases the same atoms and the same number of them, combined one with another in the same manner. Consequently the difference must be due to a difference either in the relative position of the atoms or in their movement. To consider preferably the former case, the origin of the observed isomerism has been looked for in a difference as to the relative position of the atoms. Now there is an objection to be met at starting, namely, that an accurate knowledge of the relative positions of the atoms should also take into account their movements, the existence of which is at least as probable as the existence of the atoms themselves. Everything, however, tends to show that there is a periodicity in atomic movements, and hence in a preliminary investigation we need only consider the relative position of the atoms in one phase of their movement, leaving out of consideration the movement itself.

The asymmetric Carbon Atom.—To arrive at the fundamental idea we must now consider the different possibilities as to the relative positions of the four groups which are attached to the carbon atom in virtue of its tetratomicity.

Supposing in the first place that the relative position of the four groups is represented in a plane as indicated

by Fig. I., we are led inevitably to consequences not justified by experience. In this case every compound, as for example $C(R)_2(R_2)_2$, containing carbon united to groups of which three are not identical could give rise to two forms as indicated by Figs. II. and III.; consequently such a compound as chloride of methylene, CH_2Cl_2, ought to offer a case of isomerism, and the isomers would be the more numerous when the groups R were different.

To avoid having to account for such a large number of isomers there is only one supposition possible, namely, that the four groups united to carbon occupy the angles of a regular tetrahedron at the centre of which the carbon atom itself is situated.

The only isomerism to be expected in this case presents itself when the four groups attached to the carbon atom are different ($CR_1R_2R_3R_4$). In this case only we can predict the possibility of two different relative positions as the two nonsuperposable Figures IV. and V. indicate.

This supposition therefore requires an isomerism in the case of bodies which contain such a carbon atom, an isomerism which the ordinary structural formula is incapable of predicting.

Now there follows the coincidence that tartaric acid ($CO_2H.CHOHCHOH.CO_2H$) and lactic acid ($CH_3.CHOH.CO_2H$), which offered an inexplicable case of isomerism, contained also an atom of carbon united to four different groups. It was called the 'Asymmetric Carbon atom,' because there exists no plane of symmetry in the grouping, such a plane of symmetry only presenting itself when at least two of the four groups are identical.

The asymmetric carbon atom will henceforth be expressed by italics in the formulae employed, as it has already been in the formulae of tartaric and lactic acids.

The fundamental conception of the theory consists then in the prediction of isomerism in the case of compounds containing an asymmetric carbon atom.

Graphic representation.—To thoroughly grasp the difference between the two groupings in question we can employ two tetrahedrons of cardboard cut and fastened in the manner represented in Figs. VI. and VII.; the four different groups situated at the angles of the tetrahedrons are indicated by the colours (black=n; red=r; blue=b; and white).

These models show at the same time absence of symmetry, and that their difference disappears with the disappearance of the colours; for example, if the black angle is made white both symmetry and the identity of the two tetrahedrons is produced.

Modified form of the fundamental idea.—A slightly different form may be given to the fundamental idea without making any change as to the conclusions which may be drawn from it, a form however which protects it from an objection as to its structural nature which might be raised against it.

In what has previously been stated the groups united to carbon are supposed to occupy the angles of a regular tetrahedron of which the carbon atom occupies the centre. This implies an equidistance of the four groups, which is scarcely probable when the groups are different, because such a difference implies also a difference in the forces which bind the groups to the carbon atom. This objection may be met without making any supposition as to the nature of the forces which bind the atoms, only making the assumption that these forces are equal or different according to the equality or difference of the groups attached.

This being so, the regular tetrahedron still holds good

in the case where the four groups are identical, as $C(R_1)_4$.

In the case where three groups $(R_1)_3$ are the same, and one, R_2, different, as $CR_2(R_1)_3$, the group R_2 will be nearer to or further from the centre than the others, in such a way that the three sides R_1R_2 equal each to each, have a different length from the three sides R_1R_1 also equal each to each. As to $C(R_1)_2(R_2)_2$, where the groups are equal in pairs, we can recognise three pairs of sides of different lengths indicated by R_1R_1, R_1R_2, and R_2R_2.

Again, in the case $C(R_1)_2R_2R_3$ there is only equality of two pairs of sides.

Finally, the two groupings in the case of the asymmetric carbon atom, i.e. the case $CR_1R_2R_3R_4$ are now represented by two different tetrahedrons. None of the sides are any longer equal, and the symmetry which still existed in the case $C(R_1)_2R_2R_3$ has disappeared.

We may observe in conclusion that the two forms representing the different groupings round the asymmetric carbon atom, are the nonsuperposable images one of the other (Figs. IV. and V.), such forms as are called in crystallography enantiomorphous.

II. Verification of the Fundamental Idea.

A. *General character of the isomerism caused by the asymmetric carbon atom.*

The theory then of the asymmetric carbon atom leads to the prediction of an isomerism in the case of bodies containing an atom of carbon united to four different groups. This isomerism is observable in the case of the tartaric and lactic acids, as has been stated, and in a large number of other cases to be mentioned. Before entering into details we may notice that the isomerism

in question, proceeding according to our theory from a special cause, namely, the relative position of the atoms, presents also a perfectly distinct character in comparison with the isomerisms due to a different cause, such as molecular structure.

The former isomerism is always characterised in a constant and special manner by two properties, namely, by the rotatory power and by the crystalline form of the bodies in question.

Rotatory power.—As to rotatory power, the two isomers existing in virtue of the asymmetric carbon atom rotate the polarised ray in the liquid state, or in a state of solution, a property which bodies not containing the asymmetric carbon atom never display under the same circumstances. This rotation is a criterion of the existence of the isomerism, for it is produced with equal intensity and in an opposite sense by the two bodies. We may observe that this difference in rotatory power is accompanied in other cases also by that enantiomorphism of form or structure which we suppose to exist here. It is the case with crystals having rotatory power, such as quartz, where the opposite sign in their action on light accompanies enantiomorphism in form. It is the same with transparent bodies twisted in right and left spirals, which by that means obtain rotatory powers of different sign in the two cases. The same phenomenon also is to be noticed in the active piles of Reusch, obtained by crossing at an angle of 60° very thin plates of biaxial mica [1].

Crystalline form.—As regards crystalline form, the two isomers existing in virtue of the asymmetric carbon present hemihedral enantiomorphous forms as indicated by Figs. VIII. and IX., which represent the crystalline form

[1] Wyrouboff, Ann. de Chim. Phys. (6) viii. 340.

of dextro and laevo bimalate of ammonium ; the external appearance of the two modifications offers a difference absolutely analogous to that which we have supposed due to the atomic grouping; they are each the non-superposable image of the other.

We may add that Pasteur has already pronounced the opinion that the rotatory power and special crystalline form of the bodies in question must result from an unsymmetrical grouping in the molecule ; on this question he expresses himself in the following terms [1] :—

'Are the atoms of the dextroacid (tartaric) grouped in the spirals of a right-handed helix or *situated at the angles of an irregular tetrahedron*, or arranged in such or such particular unsymmetrical fashion? We are unable to reply to these questions. But there can be no reason for doubting that the grouping of the atoms has an unsymmetrical arrangement with a nonsuperposable image. It is not less certain that the atoms of the laevo-acid realise precisely an unsymmetrical arrangement the inverse of the above.'

Again, by mathematical means we are able to deduce from the dissymmetry of the constituents the necessary existence of rotatory power, as also from defect of symmetry in the characteristic enantiomorphous crystalline form [2].

B. *Proofs of the coincidence of a special isomerism with the presence of asymmetric carbon.*

From the researches of Pasteur on active bodies we are entitled to assert that the existence of a compound which in the liquid state or in solution deflects the plane of polarisation, necessarily entails the existence of an

[1] Leçons de Chimie, 1860, 25.

[2] E. Sarran, Journ. de Math. pur. et appl. (2) xii. 1867.

isomer which differs from it by the sign of its rotation and by its enantiomorphous crystalline form.

Pasteur has recognised this co-existence in the case of the tartaric acids and their derivatives. There is also a whole series of analogous observations in addition. The case is the same with camphoric acid, camphor, borneol, spirit of turpentine, campholurethane, amyl alcohol, malic acid, asparagine and its derivatives, mandelic acid, tyrosine, glutamic acid, &c. For particulars we may refer to the work of Chautard on the two camphoric acids [1], Haller on the derivatives of the two camphors [2], and Piutti on the derivatives of the two asparagines [3].

Hence the existence of every compound possessing rotatory power in the liquid or dissolved state implies a case of this special isomerism which we have in view, whether the isomer has actually been obtained or not: consequently it is necessary to prove that optical activity in the circumstances described entails the presence of an asymmetric carbon atom.

In this demonstration two possible points of view will be chosen for examination: 1st, *The atomic structure of bodies having rotatory power*, and 2nd, *the properties of bodies which have an asymmetric carbon atom.*

(1) *Atomic structure of bodies which in the liquid or dissolved state possess rotatory power.*

Presence of an asymmetric carbon atom in every active body.

The preceding statements lead to a necessary condition in the atomic structure of bodies having rotatory power, namely, the presence of an asymmetric carbon atom.

[1] Jahresber. 1863, 556. See also Jungfleisch, Bull. Soc. chim. xix. 290, 530.
[2] Bull. Soc. chim. xli. 327; Compt. rend. civ. 66.
[3] Compt. rend. ciii. 134.

Original proofs.—Before giving the verifications which the theory has received in this respect in the fourteen years since its initiation, we will begin by inserting the original list of active bodies whose atomic structure was then known.

Ethylidine lactic acid $CH_3.CHOH.CO_2H$.
Aspartic acid $CO_2H.CHNH_2.CH_2.CO_2H$.
Asparagine $CO_2H.CHNH_2.CH_2.CONH_2$.
Malic acid $CO_2H.CHOH.CH_2CO_2H$.
Malamide $CONH_2.CHOH.CH_2.CONH_2$.
Amyl-alcohol $C_2H_5(CH_3)CH.CH_2OH$.
Valeric acid $C_2H_5(CH_3)CH.CO_2H$.
Amylamine amyl chloride, &c.
Amylethane $C_2H_5(CH_3)CHC_3H_7$.
Active caproic acid $C_2H_5(CH_3).CH.CH_2.CO_2H$.
The glucoses $CH_2OH(CHOH)_4COH$.
Mannite and dulcite $(CH_2OH)(CHOH)_4(CH_2OH)$.
Saccharic acid $CO_2H(CHOH)_4CO_2H$.

The carbohydrates, cane sugar, milk sugar, starch, dextrine, &c., contain as compound ethers of the preceding, the asymmetric carbon atoms which the bodies themselves contain.

The same reasoning applies to the glucosides.

Camphor, according to Kekulé's formula, borneol, spirit of turpentine.

Camphoric acid and some other camphor derivatives where the asymmetry of the carbon is maintained.

New proofs.—This list has since been extended in the most satisfactory way.

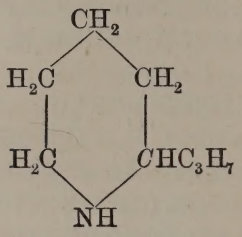
We will take first those compounds whose optical activity was then known, but whose constitution was doubtful but has since been ascertained; in this category come—

Oxyglutaric acid $CO_2H.C_2H_4.CHOH.CO_2H$.

Glutamic acid $CO_2H.C_2H_4\,CHNH_2\,CO_2H$.

Quinic acid $C_6H_7\,(OH)_4CO_2H$.

And we may add Conine, the first and so far the only alkaloid whose constitution has been determined by analysis and synthesis, thanks to the researches of Hofmann [1] and Ladenburg [2]; the optical activity of this body is explained by the presence of the asymmetric carbon atom in the constitution assigned to it:



We will now instance certain compounds whose constitution allowed the prediction of optical activity, which activity had not however at that time been observed.

Thus Le Bel has been able to obtain:—

Active secondary amyl alcohol [3] $C_3H_7CHOH\,CH_3$, from an inactive mixture of the same constitution;

Active secondary iodide of amyl $C_3H_7CHICH_3$, prepared from the preceding compound [4];

Active propylene glycol [4] $CH_3.CHOH.CH_2OH$, obtained from the inactive mixture of the same composition;

Active oxide of propylene $CH_3CH(O)CH_2$, from the preceding compound.

[1] Berl. Ber. xviii. 5.

[2] Ib. xix. 2578.

[3] Bull. Soc. chim. (2) xxxiii. 106.

[4] Ib. xxxiv. 129.

Lewkowitsch[1] has succeeded in obtaining:—

Active glyceric acid $CH_2OH.CHOH.CO_2H$, obtained from an inactive mixture of the same constitution.

The same chemist[2] discovered the activity of—

Mandelic acid $C_6H_5CHOH\,CO_2H$, obtained by treating amygdaline with hydrochloric acid.

Mauthner has studied the following bodies in consequence of the presence of asymmetric carbon in them and discovered the optical activity of cystine $CH_3CSH\,NH_2CO_2H$[3], tyrosine $C_6H_4OH.CH_2CH\,NH_2CO_2H$[4], leucine $C_4H_9.CH.NH_2.CO_2H$[5].

The optical activity of these three bodies, products of living organisms, was in a high degree probable from the theory; the more so as Erlenmeyer and Hell[6] in describing the absence of rotatory power in leucine were able to observe it in the case of valeric acid derived from leucine. The substances mentioned were regarded as inactive till the researches of Mauthner, because of the weakness of the solutions which were employed. We may add that after the publication mentioned, Külz[7] observed the activity of cystine, while Schulze, Barbieri, and Bosshard[8] confirmed that of tyrosine and leucine.

Külz[9] also observed the optical activity of oxybutyric acid $CH_3.CHOH.CH_2.CO_2H$, discovered in the urine of diabetic patients by Minkowski[10], who himself confirmed Külz's observation[11].

In conclusion, mention may be made of bodies lately

[1] Berl. Ber. xvi. 2720.
[2] Ib. 1565.
[3] Sitz. Ber. der Ak. d. Wiss. Wien (2), lxxxv. 882.
[4] Loc. cit.
[5] Zeitsch. f. physiol. Chem. vii. 222.
[6] Ann. Chem. Pharm. clx. 285.
[7] Berl. Ber. xv. 1401.
[8] Zeitsch. f. physiol. Chem. ix. 103.
[9] Berl. Ber. xvii. Ref. 534.
[10] Loc. cit. xvii. Ref. 334.
[11] Loc. cit. xvii. Ref. 535.

discovered, which by the presence of asymmetric carbon and by their rotatory power afford a signal instance of this coincidence.

The substances are—

Phenyl cystine $CH_3.CS(C_6H_5)NH_2.CO_2H$.

Bromophenyl cystine $CH_3CS(C_6H_4Br)NH_2.CO_2H$.

These bodies, obtained by Preusse and Baumann as products of decomposition of an acid contained in the urine, after the introduction of bromobenzene into the organism, had not been studied as to their optical character till Külz[1] drew attention to the matter after his discovery of the rotatory power of cystine; then the same property was recognised in the former bodies by the physiologists mentioned[2].

To the researches of Ladenburg[3] we are indebted for active α-pipecoline and active α-ethylpiperidine.

These compounds have been obtained from their inactive mixtures respectively; their constitution corresponds to that which has been given for conine, the group propyl being replaced by the groups methyl and ethyl.

Let us add finally—

Arabinose $CH_2OH(CHOH)_3COH$.

Tetroxyvaleric acid derived from it by oxidation[4].

Saccharine, the lactone of the acid $CH_2OH(CHOH)_2COH(CO_2H)CH_3$[5].

Hexylic alcohol of Roman camomile[6] $C_2H_5(CH_3)CHCH_2CH_2OH$, giving on oxidation dextro-hexylic acid, corresponding to the laevo acid obtained by means of amyl iodide[7].

[1] Berl. Ber. xv. 1401. [2] Ib. xv. 1731. [3] Ib. xix. 2584, 2975.
[4] Berl. Ber. xix. 3031, xx. 339. [5] Ib. xviii. 1333, 2608.
[6] Van Romburgh, Rec. des Trav. chim. des Pays-Bas, vi. 150.
[7] Wurtz, Ann. Chim. (3) li. 358.

Phenylamidopropionic acid $C_6H_5.CH_2.CHNH_2.COOH$ and trioxybutyric acid $CH_2OH(CHOH)_2CO_2H$[1].

Phthalylamidocaproic acid $C_6H_4C_2O_2:N.CH.C_4H_9COOH$ and leucinephthaloylic acid[2].

Galactocarbonic acid $C_7H_{14}O_8$[3].

Refutation of Contradictory Observations. — From time to time observations not in accord with the theory have been reported, but experience has constantly demonstrated their inaccuracy. The following compounds for instance :—

Propyl alcohol $CH_3.CH_2.CH_2OH$, reported active by Chancell[4].

Styrolene of Storax $C_6H_5.CH.CH_2$, reported active by Berthelot[5].

Iodide of trimethyl-ethyl-stibine $(CH_3)_3\ C_2H_5\ SbI$, reported active by Friedländer[6].

β-picoline $NC_5H_4.CH_3$, reported active by Hesekiel[7].

As to propyl alcohol, its apparent activity was due, according to Henninger[8], to amyl alcohol.

As to styrolene, I have been able to show[9] that its rotatory power is due to the presence of an active body of different composition.

This body it is possible to isolate by repeated distillation of ordinary styrolene. A certain quantity of metastyrolene formed by the heat remains each time in the retort, and a liquid collects in the receiver, having a higher rotatory power, the value of which agrees with

[1] Journ. Chem. Soc. abs. 1887, 369, and Ann. Chem. Pharm. ccxlv. 294.
[2] Ann. Chem. Pharm. ccxlii. 9, and Berl. Ber. xxi. 277.
[3] Compt. rend. cvi. 286.
[4] Ib. lxviii. 659, 726.
[5] Ib. lxiii. 518.
[6] Journ. f. Prakt. Chemie, lxx. 449.
[7] Berl. Ber. xviii. 3091.
[8] Private communication.
[9] Maandblad voor Natuurwetenschappen, vi. 72; Berl. Ber. ix. 5.

that calculated from the original styrolene, as the following experiments show:—

First distillation: 25 grams of the original styrolene, rotating $-5^{\circ}\cdot54$, give on distillation a residue of metastyrolene, and in the receiver 16.6 grams of a liquid rotating $-8^{\circ}.36$. Calculated from the original styrolene,

$$-5^{\circ}\cdot54 \times \frac{25}{16.6} = -8^{\circ}.34.$$

Second distillation: 16.4 grams of the liquid rotating -8.36 give on distillation 5.5 grams of metastyrolene, and in the receiver a liquid rotating $-12^{\circ}.67$. Calculated from the styrolene distilled $-8.36 \times \frac{16.4}{16.4-5.5}$ $= -12^{\circ}.58$.

A third distillation after preliminary heating gave, besides metastyrolene, a liquid entirely different from styrolene both in properties and in composition.

Since Berthelot[1] adheres to his original opinion, time must decide the question.

Three chemists have since then occupied themselves with styrolene of storax, and all of them have recognised the impurity which I had reported.

Krakau[2] found a very notable variation in the rotation of styrolenes of different origin. While Berthelot found -3°, and I found $-5^{\circ}.5$, Krakau obtained specimens rotating from $-0^{\circ}.6$ up to $-6^{\circ}.8$. He observed also that as the activity of styrolene diminishes, its specific gravity approximates to that of cinnamene, that is to say of artificial inactive styrolene, while its aptitude for polymerisation becomes more marked, as shown by the increase of specific gravity, which styrolene experiences on keeping. See the following table:—

[1] Compt. rend. lxxxii. 441.

[2] Berl. Ber. xi. 1259.

Rotation.	Specific gravity.	Sp. gr. after one year.
$-0°.6$	0·926	0·936
$-3°.6$	0·915	0·921
$-5°.6$	0·911	0·914
$-6°.8$	0·912	0·914

Von Miller[1] states that a specimen of styrolene obtained by him rotated as much as $-38°.03$, and had at the same time a composition quite different from C_8H_8 and a much lower specific gravity (0.8978).

Finally, Weger[2] confirmed that what is called styrolene of storax, is a mixture from which it is not possible even by repeated fractionations to isolate pure styrolene.

From the above, it follows that the observation of Berthelot is a by no means decisive objection to the theory in question.

As to the iodide of trimethyl-ethyl-stibine, Le Bel[3] has proved that the activity in this case also is due to an impurity, probably introduced with the ethyl alcohol. Prepared from ethyl alcohol, previously heated in the form of ethylate of soda, to render inactive the traces of amyl alcohol which might accompany it, the product does not evince any rotatory power.

As to β-picoline obtained by means of acetamide and pentoxide of phosphorus, Landolt[4] has been able to attribute its activity to an error of observation.

To the preceding examples may also be added papaverine, reported active by Hesse[5]. Goldschmiedt, however[6], determined the formula of papaverine, and

[1] Berl. Ber. xi. 1450.
[2] Ann. Chem. Pharm. ccxxi. 68.
[3] Bull. Soc. chim. xxvii. 444.
[4] Berl. Ber. xix. 157.
[5] Ann. Chem. Pharm. clxxvi. 198.
[6] Sitz. Ak. Wiss. Wien, Jan. 1888.

found it to contain no asymmetric carbon atom. Examining then the optical behaviour, he found it inactive, and attributed Hesse's observation to impurity.

The activity disappears with the Asymmetric Carbon Atom.—There is a third class of observations particularly conclusive in the verification of the relation between rotatory power and the asymmetric carbon atom. In the original pamphlet attention was directed to certain cases then known, where the optical activity disappears in certain derivatives of active bodies when the asymmetric atom is no longer present. In illustration of this, we were then able only to instance the following:—

Malonic, fumaric, and maleic acids, inactive derivatives of active malic acid; tartronic acid inactive, a derivative of tartaric acid active; cymene inactive, derived from camphor active.

Since then we have become acquainted with a large number of analogous instances.

We shall consider first two groups, the amylic series, and the derivatives of succinic acid, relating to which researches have been carried in all directions.

In the amyl series derivatives of the active alcohol $CH_3(C_2H_5)CH.CH_2OH$ retain their activity in the ethers and amyl sulphates, in the chloride, bromide and iodide, in amylamine and its salts, in the aldehyde and valeric acid, in the cyanide and in caproic acid, in amylethane and in diamyl. Without the guidance of the theory we might suppose that the activity would be retained in all cases; but guided by the theory, Le Bel[1] and, later, Just[2] have examined those immediate derivatives where the asymmetric carbon atom is no longer present. They were on the one hand amyl methane

[1] Bull. Soc. chim. (2) xxv. 565.
[2] Ann. Chem. Pharm. ccxx. 146.

$(C_2H_5)_2CH\,CH_3$ and amylene $CH_3(C_2H_5)C.CH_2$, and on the other amyl hydride $(CH_3)_2CHC_2H_5$. Rotatory power is wanting in the case of each of these three bodies.

The same peculiarity occurs in the derivatives of succinic acid. Starting from active tartaric acid, we know that the rotatory power is retained in its salts and ethers, in tartramic acid and tartramide, in malic acid, its salts, ethers, and amide, but the activity disappears in succinic acid, $CO_2H.CH_2.CH_2.CO_2H$, obtained by reduction of malic acid [1], and in chloromaleic acid, $CO_2HC\,ClCH\,CO_2H$ [2], obtained by treating tartaric acid with pentachloride of phosphorus; in these compounds also the asymmetric atom is no longer present. Starting from active asparagine we know that the rotatory power is retained in its salts, in aspartic acid and its salts, in malic acid its salts and ethers, in uramidosuccinic acid, and urimidosuccinic acid [3]; but the activity disappears in succinic acid, which can be obtained from asparagine [4].

There remain to be mentioned several special confirmatory cases:

Oxalic acid, obtained from active sugar [5] or from active tartaric acid [6], is destitute of rotatory power; the same is the case with furfurol obtained from active carbohydrates [7]. Active phenyl cystine furnishes by treatment with baryta, inactive phenyl mercaptan [8]. The active oxybutyric acid of Minkowski and Külz furnishes an inactive crotonic acid [9].

[1] Bremer and Van 't Hoff, Berl. Ber. ix. 215.
[2] Van 't Hoff, Berl. Ber. x. 1620.
[3] Piutti, Compt. rend. ciii. 134. [4] Van 't Hoff, Berl. Ber. x. 1620.
[5] Van 't Hoff, loc. cit. [6] Loc. cit. [7] Loc. cit.
[8] Baumann and Preusse, loc. cit.
[9] Deichmüller, Szymanski and Tollens, Ann. Chem. Pharm. ccxxvii. 95.

Among the observations of this order, it appears to me that particular attention is due to the case where the product, deprived of the asymmetric carbon atom, has been obtained by fermentation, i.e. by the action of organisms, because this action, as we shall see later, is particularly favourable to the production of active bodies; consequently, if an inactive body is found under these circumstances, we have reason to suppose that this inactivity results from the incompatibility of its constitution with the possession of rotatory power.

In this category come the inactive alcohols, ethylic, propylic, and butylic, produced by the fermentation of active glucose. They had already been noticed; I have since been able to make the following additions:—

Succinic acid, obtained by fermentation of active asparagine, is inactive[1]; I have determined that the same acid, also inactive, is obtained by the fermentation of malate of lime[2], of tartrate of lime[3], and of starch[4].

Beyerinck, to whose favour I am indebted for the products obtained by Fitz, procured me also a specimen of ethyl acetate, obtained by him in a special fermentation of maltose; and Van Deventer was able to verify the inactivity of this compound.

(2) *Properties of bodies containing the asymmetric carbon atom.*

Inactivity is due to the presence of a mixture.—When a compound with an asymmetric carbon atom is produced in the vegetable or animal organism, it is found almost without exception to possess optical activity. The case is quite different when such a compound is formed artificially; in this case, without exception, optical activity is wanting. We are bound therefore to

[1] Van 't Hoff, loc. cit.
[2] Berl. Ber. xii. 474.
[3] Ib. 474.
[4] Ib. xi. 42.

remove this objection to the principles which have been enunciated.

For this purpose we will confine ourselves at present to those compounds which only contain one asymmetric carbon atom, reserving the consideration of those compounds which contain more than one such atom for a subsequent chapter.

From the first, Le Bel and I have held that the inactivity in these cases results from the presence at the same time of an equal quantity of each of the two oppositely active isomers.

Theoretical Proof.—That the production of an inactive mixture in the reactions of the laboratory was not only possible but even probable, Le Bel has shown by the following reasoning from a general principle of the calculus of probabilities [1].

'When any phenomenon can take place in two ways only, and when there is no reason for the first method to be employed in preference to the second, if the phenomenon has taken place m times according to the first method, and m' times according to the second, then the ratio $\frac{m}{m'}$ approaches unity when $m+m'$ increases indefinitely. Also, if an unsymmetrical body (containing the asymmetric carbon) is obtained by substitution from a symmetrical body (not containing the asymmetric carbon) the dissymmetry has been introduced by one of the substitutions; let us consider this case more particularly. The radical or atom, the replacement of which brought about the dissymmetry, had, previous to its replacement, a homologue in the molecule symmetrical with it, in respect to a point or plane of symmetry; these radicals finding themselves in similar dynamical and geometrical

[1] Bull. Soc. chim. xxii. 346.

conditions, if m and m' represent the number of times they are replaced respectively, $\frac{m}{m'}$ must approach unity, as the number of these substitutions increases beyond a measurable limit.

'Now if the replacement of one of the homologous radicals produces the dextro-rotatory body, the replacement of the other will give the laevo-rotatory, consequently both will be in equal proportions.

'It is the same thing with unsymmetrical bodies formed by addition; in fact the body added to the symmetrical molecule in destroying the symmetry might occupy an identical position situated at the opposite side of the point or plane of symmetry; the previous reasoning applies equally to this case.'

We may add that such a case has been known for a long time: namely, in the synthesis of tartaric acid starting from inactive compounds, such as succinic acid, it is racemic acid which is obtained. Now this acid is nothing else than a compound in equal proportions of the dextro- and laevo-tartaric acids.

Experimental Proof. Mesotomism[1].—Now since the theory admits the prediction of compounds which ought to be found in suitable circumstances,—in short, since the opinion has been stated that every inactive body having an asymmetric carbon atom must be separable into two active isomers in equal quantities, as is racemic acid,—experiment has not been slow to justify this pre-

[1] It has been considered advisable to give a specific name to the process of separating optically opposite isomers, corresponding to the French term 'dédoublement' as used in this sense. The term employed is for 'dédoublement' 'mesotomism,' for 'dédoublable' and 'non-dédoublable,' 'mesotomic' and 'amesotomic.' By employing these terms we shall be spared the necessity of paraphrasing the meaning which otherwise would be necessary, since the word 'separation' would lead to ambiguity.

diction; in fact, at the present time, no inactive compound with a single asymmetric carbon has withstood this separation.

Le Bel has effected the mesotomism of—

Propylene glycol[1] $CH_3.CHOH.CH_2OH$, obtained from glycerate of soda by M. Belohoubeck's method.

Secondary amyl alcohol[2] $C_3H_7CHOHCH_3$, by Friedel's method from butyryl methane.

Primary amyl alcohol[3], obtained by heating the sodium compound of its active isomer.

He employed, to effect the mesotomism, the method of micro-organisms, initiated by Pasteur; these organisms have an unequal aptitude for the destruction of the two isomers, and their growth for a sufficiently long time effects the production of one of these isomers from an inactive mixture. Thus, a solution containing per litre 3 grams of inactive alcohol, 1.25 grams of different salts, a little water of yeast, and slightly acidulated, is sown with the spores of the mould. After a month, the growth of a green appearance having died down, the liquor is distilled and amyl alcohol isolated rotating $+1°7'$ for 10 centimetres.

Bremer has mesotomised:—

Malic acid[4] $CO_2H.CH_2.CHOH.CO_2H$, obtained by reduction of racemic acid; and malic acid[5], obtained by Loydl's method[6] by heating fumaric acid in a solution of soda.

Bremer, in order to effect the separation, employed a second method, initiated by Pasteur, which is based on

[1] Bull. Soc. chim. xxxiv. 129. Compt. rend. xcii. 533.
[2] Bull. Soc. chim. xxxiii. 106. Compt. rend. lxxxix. 312.
[3] Bull. Soc. chim. xxxi. 104. Compt. rend. lxxxvii. 213.
[4] Berl. Ber. xiii. 351.
[5] Rec. des Trav. chim. des Pays-Bas, iv. 180.
[6] Ann. Chem. Pharm. cxcii. 82.

unequal aptitude of the two active isomers, to combine with a compound possessed of rotatory power. Thus a solution of the inactive malic acid was half neutralised by means of the active base cinchonine and allowed to crystallise in presence of a fragment of active malate of cinchonine; by that means active malate was separated.

An analogous method has resulted in the hands of Ladenburg in the mesotomism of the following compounds:—

α-pipecoline [1] $CH_3\,CH\,(NC_4H_9)$, obtained by reduction of *α*-methyl pyridine.

α-ethyl piperidine [2] $C_2H_5\,CH\,(NC_4H_9)$, obtained in an analogous manner.

α-propyl piperidine [3], or inactive conine, obtained by reduction of *α*-allyl pyridine.

In the three cases the inactive base was transformed into its bitartrate and allowed to crystallise, in the case of conine in presence of a fragment of bitartrate of the active base; in each case the bitartrate of the active base produced by separation was obtained.

On the other hand, the method of micro-organisms has been successfully applied by Lewkowitsch for the mesotomism of the following inactive compounds:—

Mandelic acid [4] $C_6H_5\,.\,CHOH\,.\,CO_2H$, from benzoic aldehyde.

Glyceric acid [5] $CH_2OH\,.\,CHOH\,.\,CO_2H$, obtained in the ordinary manner.

Lactic acid [6] $CH_3\,.\,CHOH\,.\,CO_2H$, obtained by fermentation.

We may add that Lewkowitsch [7] has also been able to effect the mesotomism of the mandelic acid just

[1] Berl. Ber. xix. 2584, 2975. [2] Loc. cit.
[3] Berl. Ber. xix. 2578. [4] Ib. xv. 1505. [5] Ib. xvi. 2720.
[6] Loc. cit. [7] Berl. Ber. xvi. 1565.

mentioned by treating it with cinchonine, as Bremer mesotomised malic acid.

It remains to be noticed that this method effects the mesotomism [1] of mandelic acid, obtained by heating its active isomer.

We may also mention the researches of Schulze and Bosshard [2]. They have employed the method of micro-organisms to mesotomise:

Inactive leucine $CH_3 . (CH_2)_3 . CHNH_2 . CO_2H$, obtained by heating albuminous substances with baryta:

Inactive glutamic acid $CO_2H . CH_2 . CH_2 . CHNH_2 . CO_2H$, obtained in the preceding manner.

Inactive aspartic acid $CO_2H . CH NH_2 . CH_2 . CO_2H$, obtained in various ways [3], has also been found mesotomic.

We may also mention asparagine, obtained by Körner and Menozzi [4] from maleic and fumaric ether. The two isomers were not actually obtained separately, but the inactive asparagine crystallised in hemihedral enantiomorphous forms.

We see then that the mesotomism of an inactive body containing an asymmetric carbon atom has been attempted no less than fifteen times, and the attempt has in no case been futile. For completeness' sake might be added the most recent proofs of possible mesotomism in the turpentine-series [5].

Impossibility of Mesotomism in absence of the asymmetric Carbon Atom.—Since therefore mesotomism has been realised fifteen times experimentally where the theory of the asymmetric carbon atom admitted of its possibility, it will not be out of place to review those

[1] Berl. Ber. xvi. 2721. [2] Ib. xviii. 388. Zeitsch. f. physiol. Chem. x. 134.
[3] Engel, C. R. cvi. 1734. [4] Berl. Ber. xxi. Ref. 87.
[5] Wallach, Ann. Chem. Pharm. ccxlvi. 225.

cases where attempts at mesotomism have failed completely in accord with the absence of the asymmetric carbon atom in the compound in question.

Taking the inactive bodies obtained by the action of organisms, as succinic acid in the fermentation of asparagine, of starch, and of tartrate and malate of lime; this acid has been obtained inactive in spite of the mesotomistic action which produced it. We may add that the attempts at separation made by Anschütz and Hintze in the case of oxalic acid [1] and of fumaric acid [2] have failed, also the attempt of Le Bel to mesotomise orthotoluidine [3].

Inactive Amesotomic type.—After the researches of Le Bel and myself had been laid before the Chemical Society of Paris, M. Berthelot [4], in offering some remarks, insisted on the insufficiency of our conceptions in that they did not take into account the 'inactive amesotomic type.'

Pasteur had made known this modification in the case of tartaric acid, where in fact we are acquainted with the active acids and their compound (racemic) and inactive amesotomic tartaric acid representing this fourth type. Now in this special case, where we are dealing with two asymmetric carbon atoms, our theory predicts, as we shall see, the existence of an inactive amesotomic compound.

Since that time several chemists have admitted the existence of this amesotomic inactive modification as a general rule.

Now, where the constitutional formula only offers a

[1] Berl. Ber. xviii. 1394.
[2] Ann. Chem. Pharm. ccxxxix. 164.
[3] Bull. Soc. chim. xxxvii. 98.
[4] Bull. Soc. chim. xxii. 339.

single asymmetric carbon atom, this type is inexplicable by the theory. On this account the objection of M. Berthelot was perfectly justified. Only it was necessary to seek for the representative of this type among those bodies which contain only one asymmetric carbon atom, and M. Berthelot quoted as such inactive malic acid, the only compound in fact which offered a grave objection to the theory.

The malic acid in question had been obtained by Pasteur from the inactive aspartic acid of Dessaignes. This malic acid was inactive, and Pasteur reported it as amesotomic [1], but it appears to me, after reading his memoir, that Pasteur did not insist on this opinion. Since then, however, the existence of inactive amesotomic malic acid, along with the inactive mesotomic compound, had been generally admitted [2].

The recent experiments of Bremer, Anschütz, and H. J. Van 't Hoff, have now removed this difficulty; not only has Pasteur's acid been subjected to a fresh examination, but all the inactive malic acids obtained by the different methods known at the present day have been identified with the inactive acid obtained by mixing equal quantities of the dextro and laevo acids, and more than one of these inactive acids has been mesotomised.

H. J. Van 't Hoff proved [3] the identity of the synthetical inactive acid with Pasteur's acid; he noticed in the acid ammonium salt of the former, the two crystalline forms observed in the case of the latter acid according as the salt is hydrated or anhydrous. He proved [4] the same to

[1] Ann. Chim. Phys. (3), xxxiv. 46.

[2] See for example Landolt, Das optische Drehungsvermögen organischer Substanzen, p. 20.

[3] Maandblad voor Natuurwetenschappen, 1885, 1 Bijdrage tot de Kennis der inactieve appelzuren. Diss, 1885.

[4] Berl. Ber. xviii. 2170.

be the case for the inactive malic acid obtained by Loydl by heating fumaric acid with soda; the mesotomism of this acid by Bremer [1] confirmed the identity.

Again, the same crystalline form has been observed [2] in the bimalate of ammonia obtained by Kekulé from bromo-succinic acid. Now by a crystallographic comparison of this salt, obtained from the acid of Pasteur, that of Kekulé, and that of Jungfleisch, prepared by heating fumaric acid with water, Anschütz [3] discovered that in these cases also there was identity. We may observe that Jungfleisch [4], without giving measurements, recognised the crystalline identity of his bimalate of ammonia with that of Pasteur.

Quite recently the proof thus furnished has been strengthened by Piutti's observation [5], who found in the inactive aspartic acid, obtained by mixing the dextro and laevo isomers, the same crystalline form as that of the aspartic acid of Dessaignes, the acid which served to produce the malic acid of Pasteur.

Again the aspartic acids obtained by action of ammonia on maleic and fumaric acids respectively are found to be identical with that of Dessaignes [6], as well as that obtained from oxalacetic ether [7].

It remains to be added that the malic acid [8] obtained by heating maleic acid with soda has again been found identical with mesotomic malic acid, a result confirmed later by the probable identity of the methyl malic and ethyl malic acids which Purdie [9] obtained on treating both fumaric and maleic acids with methylate, and

[1] Rec. Trav. chim. des Pays-Bas, iv. 180.
[2] Berl. Ber. xviii. 2713.
[3] Berl. Ber. xviii. 1949.
[4] Bull. Soc. chim. xxx. 147.
[5] Compt. rend. ciii. 134.
[6] Engel, Compt. rend. cvi. 1734.
[7] Ber. Ref. xxi. 351.
[8] Berl. Ber. xviii. 2713.
[9] Journ. Chem. Soc., 1885, 855.

with ethylate of soda. The isomerism of the unsaturated acids consequently disappears in the malic compounds derived from them.

Is the presence of the asymmetric carbon atom sufficient of itself to produce optical activity?—It is proposed to reconsider a supposition which was raised in the original paper, and which has since been sufficiently tested by experience to allow of a definite expression of opinion on it. When I brought forward the necessity of isomerism in the case of the asymmetric carbon atom, it did not appear to me that this isomerism should necessarily and without exception be distinguished by the presence of rotatory power. In short it appeared to me possible *a priori* that the difference of the four groups combined with the same carbon atom was of itself insufficient to cause activity, and that some special condition in the groups themselves must be looked for. However, since then, the great diversity of active bodies with which we have become acquainted, appears to exclude any such restriction, and the difference of the groups alone appears sufficient. In fact it was clear from the beginning in virtue of the activity of lactic, malic, and aspartic acids

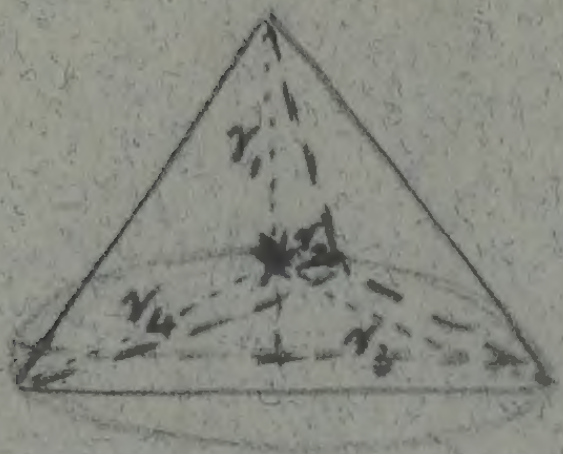
$$C\begin{cases}H\\OH\\CH_3\\CO_2H\end{cases} \qquad C\begin{cases}H\\OH\\CO_2H\\CH_2CO_2H\end{cases} \qquad C\begin{cases}H\\NH_2\\CO_2H\\CH_2CO_2H\end{cases}$$

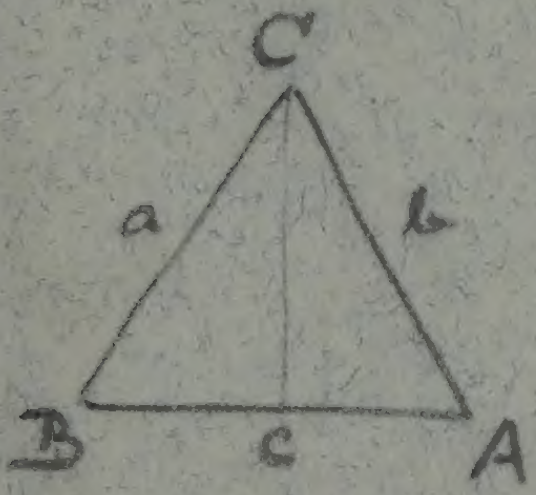
for example that any kind of variation in the carbonaceous groups was sufficient to produce rotatory power, as also the difference between them and hydrogen and between hydrogen and the oxygenated (OH) and azotised (NH_2) groups.

Since then the discovery of the activity of secondary amyl iodide $C\begin{cases}H\\I\\CH_3\\C_3H_7\end{cases}$ by Le Bel[1] has proved the difference between hydrogen and a halogen atom also to suffice for the production of rotatory power, and no restriction appears to be further necessary.

Production, by heating the active derivatives, of compounds inactive by compensation. — The loss of rotatory power by heating active bodies has been observed for some time, and the production of racemic acid in this way from dextro-tartaric acid[2] has taught us that in this case at least the loss of activity results from a partial transformation into the oppositely active isomer. Observations of this kind have recently accumulated: the heating of active amyl alcohol (in its sodium compound) produces an inactive isomer, which has been mesotomised by Le Bel[3]; from mandelic acid, an inactive isomer has been obtained and has been mesotomised by Lewkowitsch[4]; Schulze and Bosshard[5] have obtained by heating leucine an inactive isomer which they have succeeded in proving to be mesotomic; and since we must admit that the aspartic acid of Dessaignes is mesotomic, we may add to this series the formation of inactive aspartic acid by Michael and Wing[6] by heating its active isomer: these chemists have, in fact, confirmed the identity of their acid with that of

[1] Bull. Soc. chim. (2) xxxiii. 106.
[2] Jungfleisch, Compt. rend. lxxv. 439, 1739.
[3] Bull. Soc. chim. xxxi. 104; Compt. rend. lxxxvii. 213.
[4] Berl. Ber. xv. 1505. [5] Ib. xviii. 388; Zeitsch. f. physiol. Chem. x. 134.
[6] Berl. Ber. xviii. 2984.





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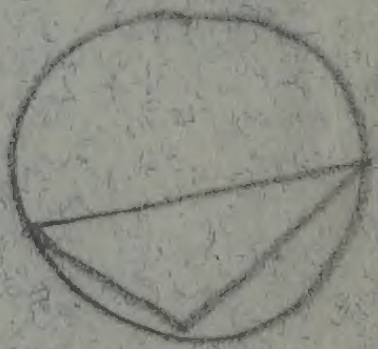

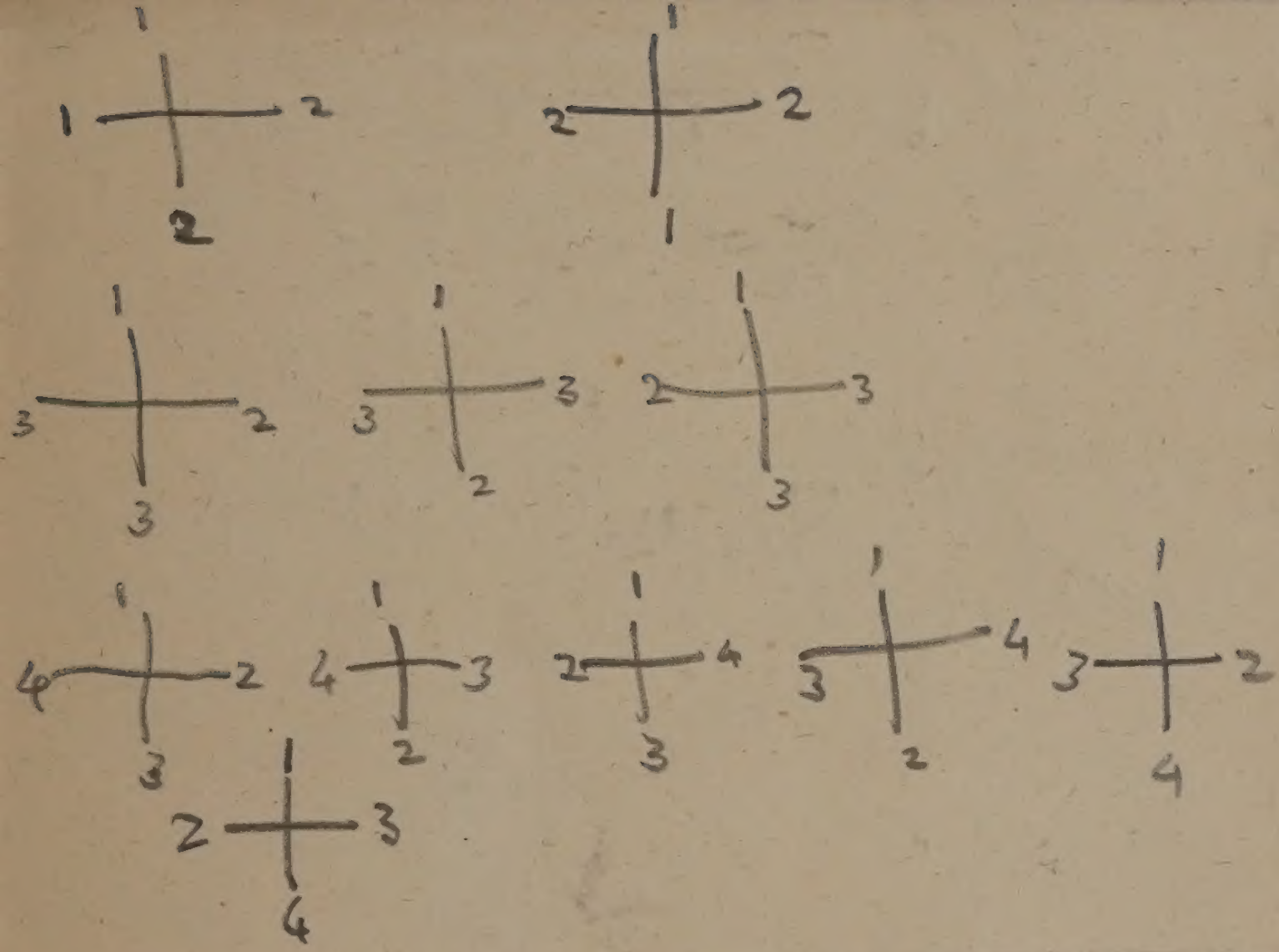
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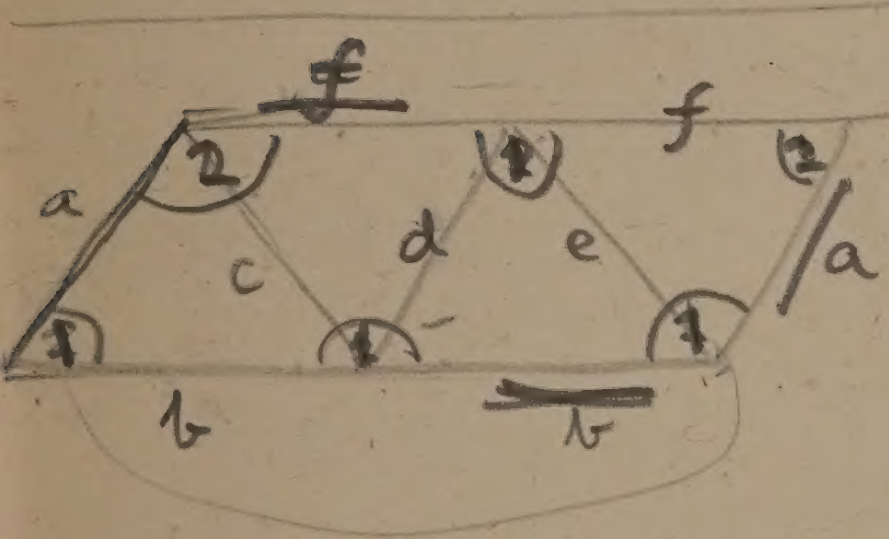
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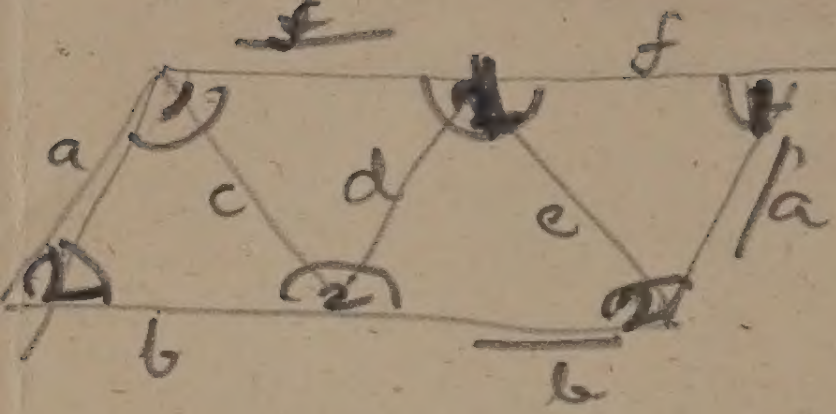

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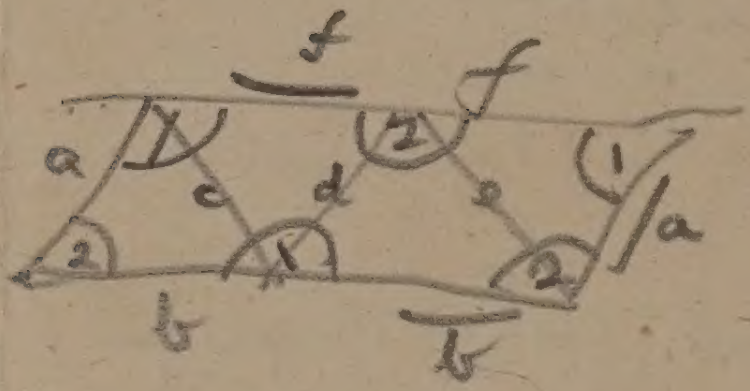

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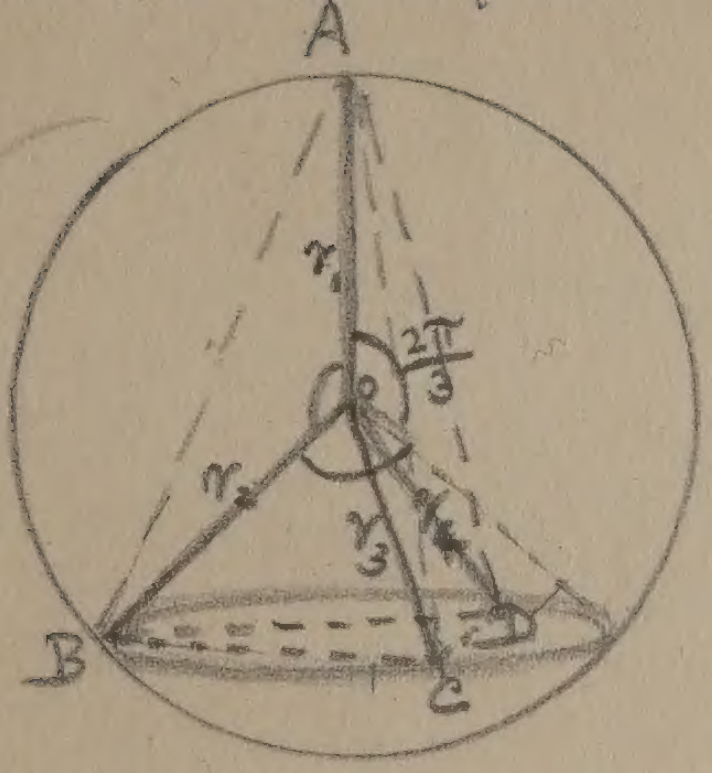


$AB = \sqrt{r_1^2 + r_2^2 - 2 \cdot r_1 \cdot r_2 \cdot \cos\frac{2\pi}{3}}$

$AC = \sqrt{r_1^2 + r_3^2 - r_1 r_3}$

$AD = \sqrt{(r_1, r_4)}$

$BC = \sqrt{(r_2, r_3)}$

$BD = \sqrt{(r_2\ r_4)}$

$CD = \sqrt{(r_3\ r_4)}$

$r_1 : r_2 : r_3 : r_4 :: 3 : 4 : 5 : 6$

d. $(R_1)_4$. $(r_1)_4 = 3.3.3.3$

$\rho_1 = \dots = \rho_6$.

$AB = \dots = \sqrt{18 - 18k}$

c. $(R_1)_3 . R_2$. $(r_1)_3 . r_2 = 3.3.3.4$

$AB = \sqrt{18 - 18k}$

$AC = \sqrt{18 - 18k}$

$AD = \sqrt{25 - 24k}$

$BC = \sqrt{18 - 18k}$

$BD = \sqrt{25 - 24k}$

$AD = \sqrt{25 - 24k}$

c. $(R_1)_2 . (R_2)_2$. $(r_1)_2 . (r_2)_2 = 3.3.4.4$

$AB =$

$AC =$

$AD =$

$BC =$

$BD =$

$CD =$

Dessaignes. From these observations we have ground for asserting that many active bodies lose their activity by heat, and that in the case of the presence of a single asymmetric carbon atom in the molecule, there results a formation in equal quantities of the two oppositely active isomers.

It is in virtue of this transformation that in the derivatives of an active compound the rotatory power more than once has been found to disappear, though the asymmetric carbon atom is still present, as for example in the production of tyrosine, leucine, and glutamic acid, by heating albuminous matter with baryta. Schulze and Bosshard did not hesitate to seek the origin of this anomaly in the explanation here offered, and found on decomposing the albuminous matter at a lower temperature by hydrochloric acid that the leucine, tyrosine and glutamic acid so obtained were active. This, taken with the direct observation of the loss of rotatory power by heating leucine, leaves no room for doubt as to the origin of the inactivity of this body obtained in the manner above described. We may add that the inactivity of pyro-tartaric acid for example, obtained from the active tartaric acid, gives rise to considerations of an absolutely analogous character.

Now there is another point of view which increases the interest of the preceding observations, since it is possible, by applying the principles of thermodynamics based on the theory of the asymmetric carbon atom, to explain this transformation with loss of activity. In respect of this demonstration I mention, referring for details to a work on chemical equilibrium [1], the conditions on which such a state of stability is dependent.

[1] Van 't Hoff, Archives Néerl. 1886. Kon. Svenska akad. Handl. 1886.

The question is of this kind: given the existence of two isomers of opposite optical activity, and the possibility of their mutual transformation, to find out the relative quantities in which these two compounds must exist together to form a stable system.

This equilibrium depends on the work (E) which the transformation can accomplish, work which must be equal to zero in the case in question, in view of the perfect mechanical symmetry of the two isomers, according to the developed conception.

It follows that the constant of equilibrium (K), which determines the relative proportions of the two compounds, is equal to unity, because this constant is related to the work (E) by the following equation :—

$$1.\ K = \frac{-E}{2T}$$

where T indicates the absolute temperature. It is clear then that to produce equilibrium the relative quantities of the two isomers must be equal.

We arrive at the same conclusion looking at the problem from the dynamical side [1]: the tendency of the transformation being the same for the two isomers, in view of their perfect mechanical symmetry, as long as one predominates the excess of it will undergo transformation.

[1] Van 't Hoff, Berl. Ber. x. 1620.

SECOND PART.

THE SINGLE LINKING OF CARBON.

I. Application of the Fundamental Idea.

Relative position of the six groups combined with carbon in the case of single linking.—In view of the development of the theory, it is necessary to have a clear conception of the structure of bodies in which the atoms of carbon are united in what is called single linking.

The fundamental principle of the tetrahedric grouping requires that the two atoms of carbon shall occupy at the same time the centre of one of the tetrahedrons and an angle of the other. This condition leads consequently to the relative position of two tetrahedrons indicated by Fig. x. for the compound $C(R)_3 C(R_1)_3$, but every different relative position derived from this by rotation of one of the tetrahedrons about the axis CC will be equally admissible.

To avoid the prediction of an isomerism which at first sight appears endless, it is not necessary to introduce any additional hypothesis; the difficulty disappears at once if we take into account the mutual action which must take place between the groups R and the groups R_1, united to each of the two atoms of linked carbon. In fact, if this action depends, as is the case with every

known force besides, on the distance and nature of the groups in question, there will be among the possible positions only one which corresponds to the state of stability.

For the sake of precision let us suppose this position to be that indicated by Fig. x., where the groups R and R_1 are supposed to be opposite to one another, forming thus the angles of an equilateral triangular prism. We may observe that every different supposition in this respect would lead to the same conclusions as we shall offer here.

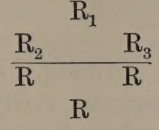
Graphic representation.—We shall introduce, before going further, a very simple notation by which the groups combined with the atoms of carbon are indicated as follows :—

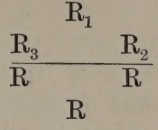
$$\begin{array}{cc} & R' \\ R & \quad R \\ \hline R_1 & \quad R_1 \\ & R'_1 \end{array}$$

The groups placed below one another in this notation are those which we suppose opposite in reality. Not to allow of any misinterpretation, it is necessary to observe that the actual position is obtained by folding the paper at right angles through R R and $R_1 R_1$, so as to raise R′ and R'_1 above the plane of the paper, the groups thus forming the angles of the triangular prism mentioned.

Asymmetry in one of the atoms of carbon.—Let us now examine the case of asymmetry in one of the carbon atoms, that is to say the case $C(R)_3 CR_1 R_2 R_3$, where the four groups $R_1 R_2 R_3 C(R)_3$ are different, with which one of the carbon atoms is combined; the isomerism existing according to the theory is expressed in our

notation by the different order of the groups $R_1R_2R_3$, as the figures below show—





This difference in the consecutive order has been indicated elsewhere [1] by two arrows in opposite directions, but we propose to introduce here a simplification. In fact we can make use of such formulae as $C(R_1R_3R_2)C(R)_3$ and $C(R_1R_2R_3)C(R)_3$, that is, the ordinary formulae, to indicate this difference, always supposing this notation to have a real signification as to the relative order of the groups $R_1R_2R_3$. It is clear that in this respect the formulae indicated present a difference absolutely analogous to that of the complicated symbols previously employed.

Asymmetry in more than one carbon atom.—The case of isomerism in presence of two asymmetric carbon atoms, i.e. the case $CR_1R_2R_3\,CR_4R_5R_6$ can be expressed by the four following symbols:—

a. (1) $CR_1R_2R_3\,CR_4R_6R_5$,
a. (2) $CR_1R_3R_2\,CR_4R_5R_6$,
b. (1) $CR_1R_2R_3\,CR_4R_5R_6$,
b. (2) $CR_1R_3R_2\,CR_4R_6R_5$,

representing pairs of nonsuperposable images, and consequently of isomers with rotatory power, equal and opposite and of hemihedric enantiomorphous crystalline form.

It is easy to see that the number of possible isomers doubles itself for each asymmetric carbon atom, and for n such atoms will be 2^n, and that these isomers are

[1] Lagerung der Atome im Raume, p. 7.

always grouped in pairs, having opposite rotatory power and enantiomorphous crystalline form.

Influence of symmetry in the formula. Inactive amesotomic type.—Before proceeding to verify these considerations, it will be well to consider the case, such as $CR_1R_2R_3\,CR_1R_2R_3$, where the presence of more than one asymmetric carbon atom is accompanied by a symmetry in the formula. The four general symbols then become—

a. (1) $CR_1R_2R_3\;CR_1R_3R_2$,
a. (2) $CR_1R_3R_2\;CR_1R_2R_3$,
b. (1) $CR_1R_2R_3\;CR_1R_2R_3$,
b. (2) $CR_1R_3R_2\;CR_1R_3R_2$.

It is clear that in this case the total number of isomers is reduced, because the symbols *a.* (1) and *a.* (2) represent identical structures. We notice also that this symbol corresponds to a body destitute of rotatory power, not by compensation of oppositely active isomers, but by its actual atomic structure; in fact the two parts of the molecule $CR_1R_2R_3$ and $CR_1R_3R_2$, being the non-superposable images one of the other, will have an equal but opposite action on polarised light. Thus then our theory supplies the inactive amesotomic type, isomeric with two others, *b.* (1) and *b.* (2), which have equal and opposite rotatory power.

We may here draw attention to the fact that the observation in the special case of two asymmetric carbon atoms applies equally to a greater number of such atoms, provided the essential condition, symmetry in the molecular formula, is realised. Generally, therefore, if there are n atoms of asymmetric carbon, we are led to predict, instead of 2^n active isomers, which is the case without

symmetry in the formula, the following different compounds, namely :—

$\frac{1}{2}\ 2^n$ active isomers grouped in pairs of equal and opposite rotatory power and enantiomorphous crystalline form,

and $\frac{1}{2}\ 2^{\frac{n}{2}}$ representatives of the inactive amesotomic type.

II. Verification of the Theory.

Symmetry in the formula, accompanied by the presence of two asymmetric carbon atoms.—In the case in question the theory accounts for the existence of three isomers, two having rotatory power equal and opposite, while the third will be deprived of this property without being at the same time mesotomic. We must also add that the two active isomers may produce a mixture or compound deprived of rotatory power, but clearly distinguished by its capability for mesotomism. Let us now consider the compounds which realise these conditions.

The tartaric acids.—In this respect the theory receives its most complete verification from the isomerism of the tartaric acids

$$CO_2H.CHOH.CHOH.CO_2H.$$

There are known two isomers with equal and opposite rotatory power, represented, according to the above demonstration, by the following symbols—

$$C(H.OH.CO_2H)\ C(H.OH.CO_2H)$$

and $$C(H.CO_2H.OH)\ C(H.CO_2H.OH)$$

together with their inactive combination, racemic acid, which has been mesotomised by Pasteur. But the special feature of this case is the existence of an inactive amesotomic isomer also discovered by Pasteur, which

Przibytek[1] has quite recently endeavoured to mesotomise, but always with a negative result. This compound is possible according to our theory, and representable by the following formula:

$$C(H.OH.CO_2H)\ C(H.CO_2H.OH).$$

Erythrite.—$CH_2OH.CHOH.CHOH.CH_2OH$ may be mentioned as a second representative of the inactive amesotomic type since Przibytek[2] has shown that it produces by its oxidation inactive amesotomic tartaric acid. The constitution of erythrite also admits the possibility of inactivity without entailing the necessity for separability. It is probable that arabite CH_2OH $CHOH$ $CHOH$ $CHOH$ CH_2OH obtained by reduction of active arabinose $CH_2OH.(CHOH)_3COH$, which is destitute of rotatory power[3], is also a representative of the inactive amesotomic type of which the formula admits.

There remain to be mentioned certain compounds of a constitution similar to tartaric acid, having a symmetrical formula and two asymmetric carbon atoms. These compounds merit special attention, because they present constantly an isomerism which, inexplicable by the old theory, is a necessary consequence of ours, an isomerism analogous to that of racemic and inactive tartaric acids. If at the present time none of these isomers have been mesotomised, it is only because no serious attempt has yet been made in this direction. The following may be given as instances of this isomerism.

The dibromo- and isodibromo-succinic acids

$$CO_2H.CHBr.CHBr.CO_2H.$$

For further evidence in favour of the formula

$$COOH.CHBr.CHBr.COOH$$

and against the formula $COOH.CH_2.CBr_2.COOH$ for iso-

[1] Berl. Ber. xvii. 1412. [2] Loc. cit. fin.
[3] Berl. Ber. xx. 1233.

dibromo-succinic acid, see V. Meyer and Demuth, Berl. Ber. xxi. 264.

The isomeric dimethyl-succinic acids

$$CO_2H.CH(CH_3).CH(CH_3).CO_2H\ ^{1}.$$

The isomeric diethyl-succinic acids

$$COOH\ CH(C_2H_5).CH(C_2H_5)\ COOH\ ^{2}.$$

α- and β-diphenyl-succinic acids

$$CO_2H.CH(C_6H_5)\ CH(C_6H_5)CO_2H\ ^{3}.$$

Hydro- and isohydro-benzoin

$$C_6H_5.CHOH.CHOH.C_6H_5.$$

in connection with which may be mentioned a series of derivatives and homologues offering always an inexplicable isomerism according to the old theory.

The two bromides of erythrene (and piperylene)

$$CH_2Br.CHBr.CHBr.CH_2Br\ ^{4}.$$

The isomeric dibromides of orthodinitrostilbene

$$C_6H_4NO_2.CHBr.CHBr.C_6H_4NO_2\ ^{5}.$$

Bidesyl and isobidesyl

$$\begin{array}{l} C_6H_5.CH.CO\,C_6H_5. \\ \quad\quad\quad\quad | \\ C_6H_5.CH.CO\,C_6H_5\ ^{6}. \end{array}$$

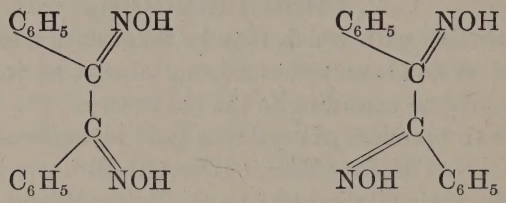
appear to belong to the same category.

The difficulty presented at first sight to the admission of the two inactive mesotomic and amesotomic types as an interpretation of the observed isomerism is singularly lessened by taking into consideration the complete analogy which exists between the formula of tartaric acid, where this interpretation is an accomplished fact, and the formulae of the bodies in question. In fact, if for the hydroxyl of tartaric acid we put in its place Br, CH_3, or C_6H_5 we

[1] Berl. Ber. xviii. 846, 2348; xx. 2736, 2988; xxii. 389.
[2] Ib. vi. 30; xiii. 473; xx. 2988, 3078; xxi. 2089, 2104.
[3] Ib. xiv. 1802; xv. 2628.
[4] Compt. rend. civ. 1446 (and B. B. xxi. 1434).
[5] Berl. Ber. xxi. 2074. [6] Ib. xxi. 1359.

arrive at the formulae of the above-mentioned substituted succinic acids, and it is far from improbable that the inactive racemic and tartaric acids submitted to these substitutions would lead to the inactive isomeric compounds.

It will not be out of place to notice here the existence of isomerism in the case of the benzil dioximes $C_6H_5 . CNOH . CNOH . C_6H_5$ [1]. According to Auwers and Meyer we have here a peculiar case of geometrical isomerism (see chap. iv.) representable by the formulae—



where, though the carbon atoms are singly linked, they are incapable of rotation about the common axis, the compounds then presenting a case of isomerism analogous to that of maleic and fumaric acids. The authors indeed state that three isomers are possible, but it will be obvious from what has been said before that if singly linked carbon atoms are not free to rotate, there will be a possibility for the existence of not three only, but an infinite number of isomers. The isomerism in question has led to the enunciation by V. Meyer and Rieke [2] of a theory of electro-chemical affinities which it will not be advisable to discuss here. The real point at issue is whether the established isomerism of the benzil dioximes is inexplicable except on the assumption of an absence of rotation in certain cases between singly-linked carbon atoms. Now the bodies in question, supposing, as is most probable, that they both have the same structural

[1] Auwers and V. Meyer, Berl. Ber. xxi. 784. [2] Berl. Ber. xxi. 946.

formula $C_6H_5.CNOH.CNOH.C_6H_5$, contain two carbon atoms, united each by one bond to C_6H_5, by two bonds to NOH, and by one bond to one another. Now we do not know the nature of the union of the carbon atoms with the NOH groups, but it is quite possible that the two bonds which effect the union are of unequal value. Hence the two carbon atoms will be asymmetric, and without being deprived of free rotation will give rise to two isomers inactive and analogous to racemic and mesotartaric acids or to hydro- and iso-hydro-benzoin. This point will however be referred to later in connection with the isomerism due to nitrogen.

III. Verification of the Theory.

More complex cases.—If among the bodies with two asymmetric carbon atoms, whose symmetrical formulae simplify the possibilities of isomerism, only one case, that of the tartaric acids, has been thoroughly investigated, it will not be thought strange to find a less complete realisation of the theoretical conceptions in more complex cases. On the other hand we are able to place in this category a host of isomerisms inexplicable by the old formulae, but necessary according to ours.

Let us consider first those *compounds whose constitutional formulae, without being symmetrical, contain two asymmetric carbon atoms.* Our theory predicts the existence of four active isomers grouped in pairs with equal and opposite rotatory power, a prediction realised in the existence of four active borneols[1] obtained by the reduction of two camphors. Now in laboratory reactions, starting from inactive bodies, we must look in the case of such compounds for the pro-

[1] Compt. rend. cv. 227.

duction of one of the two pairs mentioned, and of equal quantities of its two members, as an inactive mixture or combination. This we are acquainted with in the case of the borneols. Consequently we expect apparently only two isomers, but without rotatory power. It is also curious to notice how an inexplicable isomerism has actually been several times observed; there is, for example, always a group of this character in the bromine addition product corresponding to the formula $C(R_1R_2Br)$ $C(R_3R_4Br)$, obtained from the unsaturated isomers $C(R_1R_2)$ $C(R_3R_4)$, which will be considered more fully later. As examples may be mentioned—

The isomeric $\alpha\beta$-dibromo butyric acids $CH_3.CHBr.CHBr.CO_2H$, obtained by treating with Bromine crotonic and isocrotonic acids $CH_3.CH:CH.CO_2H$ [1].

Mesa- and Citradibromopyrotartaric acids $CH_3.CBr(CO_2H).CHBr.CO_2H$ products of the action of bromine on mesa- and citra-conic acids $CH_3.C(CO_2H):CH.CO_2H$.

The isomeric dibromo-palmitic acids $CH_3.CHBr.CHBr(C_{13}H_{25}O_2)$ products of the action of bromine on hypogaeic and gaeidinic acids $CH_3.CH:CH.(C_{13}H_{25}O_2)$.

The isomeric dibromostearic acids $CH_3.CHBr.CHBr.(C_{15}H_{29}O_2)$ obtained by the action of bromine on oleic and elaidic acids $CH_3CHCH(C_{15}H_{29}O_2)$.

The isomeric dibromobehenic acids $CH_3.CHBr.CHBr.(C_{19}H_{37}O_2)$ obtained by the action of bromine on erucic and brassidic acids $CH_3CHCH(C_{19}H_{37}O_2)$.

Let us mention here the isomeric glycols $C_6H_5.CHOH.CHOH.CH_3$ (loc. cit.), and especially the general observation to which Zincke has been led [2], that an *inexplicable isomerism regularly manifests itself among the glycols XCHOH CHOHY, an isomerism which does not appear in*

[1] Berl. Ber. xx. 1010; xvi. 1268.

[2] Berl. Ber. xvii. 708.

the case XCHOH CH_2OH ; in fact this kind of isomerism is only predicted by our theory in the first case.

We come now to the saccharic acid and the mannite groups, which both manifest symmetry in the formula accompanied by the presence of four asymmetric carbon atoms as their respective formulae indicate $CO_2H(CHOH)_4CO_2H$ and $CH_2OH(CHOH)_4CH_2OH$.

In both cases our theory predicts the following isomers:

$\frac{1}{2}2^n = 8$ active compounds grouped in pairs ;

$\frac{1}{2}2^{\frac{n}{2}} = 2$ compounds of the inactive amesotomic type.

As regards the saccharic acid group, after the recent researches of Kiliani [1] it is possible to distinguish among the bodies corresponding to the formula $(CO_2H)(CHOH)_4(CO_2H)$ no less than four isomers, namely saccharic acid, mucic, iso-saccharic, and meta-saccharic acids. Again, observing that saccharic acid has been found active [2], and that its existence implies the existence of another with equal and opposite rotatory power, the number of five isomers corresponding to the formula given is almost incontestable. Let us add that the activity of the three isomers which have not been studied in this respect is probable, and especially in the case of meta-saccharic acid, a circumstance which would materially increase the number of ascertained isomers.

In the mannite group there are to be mentioned mannite and dulcite as well-known isomers corresponding to the formula $CH_2OH(CHOH)_4CH_2OH$. Moreover, mannite having been found optically active, there is no doubt but that its optically opposite isomer will one day be discovered. It is the same for dulcite, although at present activity has only been observed in its derivatives [3].

[1] Berl. Ber. xx. 339. [2] Ann. Chem. Pharm. ccxx. 356.

[3] Compt. rend. lxxiv. 665.

It is to be noticed that mannite and dulcite cannot themselves be complimentary in this respect, as the notable difference in their melting points shows, these being identical for bodies of equal and opposite rotatory power. Thus, even excepting sorbite [1], we are acquainted with four isomers at least having the same constitutional formula.

The large number of ten isomers which our theory predicts for these groups is far from being a source of any impediment, while, on the other hand, the first well-ascertained and indubitable isomerism of this character presents an insuperable obstacle to the old theory.

It now remains to consider certain circumstances with regard to *compounds with four asymmetric carbon atoms but without symmetry in the formula*; such are the isomers of gluconic acid and the glucoses, which belong to this category where our theory predicts no less than $2^4=16$ different bodies. The realisation appears still far distant, but yet, according to the last research of Kiliani [2], there are three definite acids corresponding to the formula of gluconic acid $CO_2H(CHOH)_4CH_2OH$, namely gluconic, arabinose formic, and galactonic acids. Let us add that the activity of the three acids has been proved [3], and that these compounds do not present the characters of oppositely active isomers, and hence the existence of each of them implies that of two isomers of equal and opposite rotatory power. Consequently the existence of six isomers is already assured.

With regard to the glucoses of the formula $C_6H_{12}O_6$ it is not possible at present to determine how far the new theory can be applied, inasmuch as we are but

[1] Berl. Ber. xviii. 1321.

[2] Ib. xx. 339.

[3] Ann. Chem. Pharm. ccxx. 335; Beilstein, p. 643; Berl. Ber. xix. 3034.

imperfectly acquainted with the structure of these bodies.

The recent researches of Kiliani, however, on the one hand and of E. Fischer on the other, have greatly added to our knowledge of the structural chemistry of these compounds.

From the structural point of view, we may regard the glucoses of the formula $C_6H_{12}O_6$ as falling into two classes:—

1. Those which give condensation products with phenylhydrazine, namely, osazones and hydrazones, and which, generally speaking, have the property of reducing Fehling's solution. They may be regarded as containing an open carbon chain, having an aldehydic or ketonic group.

2. Those which do not possess the above properties, but which may be considered as containing a closed carbon chain without aldehydic or ketonic groups.

The second class, of which we have an example in inosite, a derivative of hexamethylene, should not be considered as belonging to the glucoses proper; and in respect of isomerisms, which they may furnish, owing to the arrangement of the atoms in space, will be considered later in connection with the derivatives of hexamethylene.

Of the first class, we have only evidence of the existence of glucoses which possess a normal carbon chain. Now of these the old structural theory accounts for three isomers:—

1. $CH_2OH.(CHOH)_4.CHO$
2. $CH_2OH.(CHOH)_3.CO.CH_2OH$
3. $CH_2OH(CHOH)_2.CO.CHOH.CH_2OH.$

Kiliani has studied the bodies obtainable by the union of hydrocyanic acid with glucoses[1], while Fischer has

[1] Berl. Ber. xviii. 3066; xix. 221, 767, 1128; xxi. 915.

investigated the above-mentioned phenylhydrazine derivatives[1]. Now dextrose yields with hydrocyanic acid a normal carbon chain of seven atoms, while levulose gives a derivative of isoheptylic acid. Again, dextrose and levulose both yield the same osazone. Hence we should give to dextrose the formula

$$CH_2OH.(CHOH)_4.CHO$$

and to levulose the formula

$$CH_2OH.(CHOH)_3.CO.CH_2OH$$

while the osazone must have the formula

$$\begin{array}{l} CH_2OH \\ (CHOH)_3 \\ CN_2HC_6H_5 \\ CHN_2HC_6H_5 \end{array}$$

There is thus left only one structural formula for the rest of the glucoses with normal carbon linking.

Now galactose yields a hydrocyanic derivative with a normal carbon chain, but differs from dextrose both in rotatory power and in its osazone. Here then we have a case of isomerism inexplicable on any supposed difference of structure as expressed on a plane; and these two isomers, dextrose and galactose, not being optically opposite, entail the possible existence of two more. Again, sorbin or sorbinose[2], which yields on oxidation the trihydroxyglutaric acid obtainable from arabinose, has the same structural formula as levulose, $CH_2OH.(CHOH)_3.CO.CH_2OH$; and the existence of these two, not optically opposite isomers, requires the possible existence of two more.

Finally, of the two synthetic glucoses obtained by the action of baryta on acrolein dibromide[3], α-acrose yields

[1] Berl. Ber. xvii. 572, 579; xx. 821; xxi. 1805.
[2] Ib. xxi. 3276. [3] Ib. xx. 2566, 3384.

an osazone which appears to be identical with that obtained from dextrose and levulose, except that it is inactive. This osazone by suitable treatment gives back *a*-acrose, while the corresponding active osazone gives back levulose. Hence *a*-acrose is inactive levulose and has been found to be capable of being separated into its two optically opposite constituents. Fischer's work has resulted in the synthetic production of dextrose and levulose as well as of other additional members of the glucose family. For information as to the methods employed and the further relationships of the several compounds, we refer to the original papers, especially Berl. Ber. xxiii. 2114.

Glucoses corresponding to formulae :—

$CH_2OH(CHOH)_4COH$	$CH_2OH(CHOH)_3CO.CH_2OH$
mannose (dextro-)	levulose (laevo-), fruit sugar
mannose (laevo-)	levulose (dextro-)
mannose (inact.)	levulose (inact.) *a*-acrose
dextrose (dextro-), grape sugar	sorbinose (laevo-)
dextrose (laevo-)	
dextrose (inact.)	
galactose (dextro-)	

THIRD PART.

Mesotomism of Compounds inactive by Compensation. Point of Transition.

Review of Methods.—It has been observed that if an asymmetric carbon compound is produced in a laboratory reaction starting from one which is without the asymmetric atom, the optical activity introduced according to our own conceptions does not appear as such in the compound obtained because there has been produced a mixture or compound of two isomers with equal but opposite activity. We refer to pages 38–44 for the proofs which have rendered the supposition an almost incontestable truth. We propose now to pass in review the methods which have served to effect the separation of the isomers in question, chiefly to bring out facts which quite recent researches have established as to the conditions of this separation, and consequently also as to the artificial production of active compounds.

Mesotomism is possible, thanks to three methods made known by Pasteur: these we shall examine in order; they are based on the three following principles:

1. On the different facility with which optically opposite isomers are transformed by organisms;

2. On the different aptitude of such isomers to combine with an active compound and the difference of the products so obtained;

3. On the possibility of separating in certain circumstances the bodies in question by crystallisation.

Mesotomism by means of organisms.—The curious difference in the action of organisms on optically opposite isomers was discovered by Pasteur [1], who observed that the growth of Penicillium in a dilute solution of racemate of ammonia, with the addition of a trace of phosphate, resulted in the production of a solution of laevo-tartaric acid, the dextro-isomer having disappeared owing to the action of the organisms.

This more or less physiological method has furnished a very considerable amount of evidence applicable to the theory. Let us recall the details.

Le Bel, applying this principle, mesotomised the three following compounds:

1. Amyl alcohol [2], $CH_3(C_2H_5).CH.CH_2OH$, the Penicillium preferably destroying the laevo modification;

2. Secondary amyl alcohol [3], $CH_3.CHOH.CH_2.CH_2.CH_3$, the Penicillium destroying the dextro modification;

3. Propylene glycol [4], $CH_3.CHOH.CH_2OH$, separated by means of the growth of Bacterium termo, which destroyed preferably the dextro modification.

Lewkowitsch has succeeded in applying this physiological method in the following cases:

1. Mandelic acid, $C_6H_5.CHOH.CO_2H$; the above-mentioned chemist observed that according to the organism employed, either the laevo or the dextro compound is preferably destroyed. The former occurs in the growth of Bacterium termo, Aspergillus mucor and of Penicillium glaucum [5], the latter in presence of

[1] Compt. rend. li. 298.
[2] Ib. lxxxvii. 213.
[3] Ib. lxxxix. 312.
[4] Ib. xcii. 532.
[5] Berl. Ber. xv. 1505.

Saccharomyces ellipsoideus, and probably also in the growth of Penicillium in absence of air, as in the growth of an unknown Schizomycete (Vibrio ?) [1];

2. Glyceric acid [2], $CH_2OH.CHOH.CO_2H$; the Penicillium preferably destroys the dextro modification;

3. Ethylidene lactic acid [3] $CH_3.CHOH.CO_2H$; in this case the Penicillium destroys the laevo modification.

There remain to be mentioned the separations effected by Schulze and Bosshard, again based on the physiological method:

1. Leucine [4], $CH_3(CH_2)_4CH\ NH_2.CO_2H$, where the growth of Penicillium destroys the modification which in hydrochloric acid solution turns the polarised ray to the right;

2. Glutamic acid [5], $CO_2H.CHNH_2.CH_2.CH_2.CO_2H$, where the same growth produces an analogous effect.

Finally aspartic acid, $CO_2H.CHNH_2.CH_2.CO_2H$, where Engel has employed the method of micro-organisms with success [6].

We observe that this diverse aptitude of organisms in transforming optically opposite isomers appears to correspond to their faculty of producing, from inactive substances, active compounds; always supposing that the molecular structure of the latter admits of rotatory power. For example, the vegetable economy produces from inactive carbonic acid the host of active derivatives obtainable from plants, while the animal economy, in the introduction for example of inactive bromobenzene [7], produces in like manner active bromophenylmercapturic acid [8].

[1] Berl. Ber. xvi. 1568. [2] Ib. xvi. 2721. [3] Ib.
[4] Ib. xvii. 388. [5] Loc. cit. [6] Comp. rend. cvi. 1734.
[7] Zeitsch. f. physiol. Chem. v. 309. [8] Berl. Ber. xv. 1731.

Mesotomism by means of active compounds.—Pasteur, again, has observed that optically opposite isomers have an unequal aptitude for combining with an active body, and that the combinations so obtained have each of them different properties, a peculiarity doubtless in intimate relation with the different conduct of organisms towards such isomers; these organisms in fact are formed to a great extent of optically active compounds. On evaporating a solution of racemic acid, for example, neutralised by active cinchonine, the compound of the laevo-tartaric acid with the active base is seen to crystallise first, leaving the free dextro acid in the solution.

Since then this method of separation has more than once been tried.

In the first place Bremer has employed it for the mesotomism of inactive malic acid obtained both by reduction of racemic acid[1] and by hydration of fumaric acid[2]. On adding to a saturated solution of malate of cinchonine a fragment of the same salt obtained from laevo-malic acid, after a certain time the dextro-malate crystallised out in the first case and the laevo-malate in the second case, while the optically opposite malic acid remained in solution.

Finally Ladenburg has succeeded in mesotomising inactive conine[3] by adding to a saturated solution of its bitartrate a fragment of the corresponding salt of active conine. The alkaloids corresponding to conine, but containing the radicals methyl and ethyl in place of propyl, in short the inactive *a*-pipecoline and *a*-ethyl piperidine[4] were mesotomised in a similar manner by

[1] Berl. Ber. xiii. 351.
[2] Rec. des Trav. chim. des Pays-Bas, iv. 180.
[3] Berl. Ber. xix. 2578.
[4] Ib. xix. 2975.

adding to the saturated solution of their bitartrates a fragment of bitartrate of active conine.

Spontaneous mesotomism. Point of transition.—While the first method of separation is based on the action of the living organism, and the second is dependent also on life, since the active bodies which it employs are products principally of the organism, the third method, now under consideration, acts independently of life. The method is a purely chemical one, isolating the active compound without the intervention of living matter.

This third method was also discovered by Pasteur, in the fact of the separate crystallisation of the two tartrates starting from a solution of sodium ammonium racemate. There is a special interest attaching to a description of the researches which have made known the phenomena on which this method is based.

Following the historical order, we have to state that Staedel[1] obtained a double racemate of ammonia and soda on evaporating the solution which in the hands of Pasteur yielded the two tartrates.

This apparent inconsistency was removed after a profound study of the racemate in question by Scacchi[2], from which it appears that a high temperature during crystallisation is favourable to its formation, while at an ordinary temperature there is preferably a production of the two tartrates.

Now Wyrouboff[3] has succeeded in showing a perfect simplicity in the matter in question when operating in such a manner as to prevent supersaturation; in these conditions there is a well-defined limit of temperature, about 28°, so that on evaporating there is obtained

[1] Berl. Ber. xi. 1752. [2] Rendic. dell' Acad. di Napoli, 1865, 250.
[3] Bull. Soc. chim. xli. 210; xlv. 52. Compt. rend. cii. 627.

racemate or the tartrates according as the crystallisation takes place above or below 28°.

Researches which have been executed in common with van Deventer[1] have proved that we are dealing here with a particular phenomenon capable of being brought about even apart from a state of solution. It consists in this, that the mixture of the tartrates heated above 27° produces the racemate with loss of the water of crystallisation, thus—

$2C_4O_6H_4NaNH_4\,4H_2O = (C_4O_6H_4NaNH_4)_2\,2H_2O + 6H_2O$; while below this temperature the contrary takes place. The temperature mentioned corresponds to that indicated by Wyrouboff, and the transformation observed gives consequently an evident interpretation of his observations. The following phenomena are manifested in this transformation :

1. On mixing below 27° the racemate with water in the proportions given above, the pasty mass first obtained gradually solidifies until it becomes entirely a hard dry mixture of the two tartrates;

2. The mixture of the two tartrates heated above 27° in a sealed tube partly liquifies by loss of some of the water of crystallisation and formation of racemate ;

3. Finally, the expansion accompanying the formation of the racemate admits of detailed study. The dilatometer employed consists of an immense thermometer, the bulb holding a mixture of the two tartrates and being then filled up with oil, the height of which in the stem can be read off on a scale. On keeping the dilatometer for a sufficiently prolonged time at fixed temperatures, it is noticed that between 26.7 and 27.7 a slow but prolonged and very notable dilatation takes place, accompanied by a profound change in the contents of the bulb, a partial

[1] Zeitsch. f. physik. Chem. i. 173.

liquefaction and formation of well-developed crystals of the racemate. On cooling, the inverse phenomenon takes place.

The interest attached to this observation consists in this, that it places the act of mesotomism in the same category with the analogous transformations of inorganic bodies. It is in a similar manner, for example, that the formation of the double sulphate of magnesia and soda, astrakanite, from the two sulphates takes place; thus the reaction, $SO_4Mg\,7H_2O + SO_4Na_2\,10H_2O = (SO_4)_2Mg\,Na_2\,4H_2O + 13H_2O$ occurs about 21°, while below this temperature the inverse phenomenon takes place, the whole being accompanied by circumstances which recall exactly the separation described above in detail.

Now there is another observation of still wider import, which permits a comparison between the relations presented by this chemical separation and a well-known physical phenomenon, namely that of fusion and congelation. We observe that here also there takes place a mutual and total transformation of two material systems according as we pass a fixed limit of temperature. For details I refer to Berl. Ber. xix. 2142; Zeitsch. f. physik. Chem. i. 165, 227; Rec. des Trav. chim. des Pays-Bas, vi. 36, 91, 137, confining myself here to the remark, that I have chosen, in order to recall the analogy in question, the term 'point of transition' to indicate temperature limit in the chemical case, corresponding to the term 'point of fusion' as employed in physics.

We may add that the recent observations of Wyrouboff[1] show the existence of such a 'point of transition' in the case of other racemates; thus for example the same solution deposits the sodiopotassic tartrates or the corresponding racemate according as the temperature is above or

[1] Ann. Chim. Phys. (6) ix. 221.

below 3°. At this temperature, therefore, the racemate would be mesotomised into the tartrates on warming with the quantity of water necessary for crystallisation.

This third method of mesotomism or separation has only been successfully applied in the case of racemic acid. It has however been observed[1] that inactive asparagin, obtained by the action of ammonia on maleic or fumaric ether, crystallises in hemihedral enantiomorphous forms of which the two kinds are present in equal proportions.

[1] Berl. Ber. xxi. Ref. 87.

FOURTH PART.

UNSATURATED CARBON COMPOUNDS.

I. Enunciation of the Fundamental Idea.

Historical.—We have confined ourselves hitherto to the consideration only of compounds containing so-called singly linked carbon, in short—of saturated compounds. It is now time to fix our attention on the unsaturated bodies, among which those which contain the so-called double linking of carbon play the chief part. The question is more complicated than the former; for saturated compounds being derived from marsh gas CH_4, all depend on the relative position of five atoms, while the bodies in question, as they are derived from ethylene, depend on the relative position of six.

In complete accord with its more delicate nature, the solution of the problem has always been less advanced. This arises, on the one hand, in the primitive enunciation of the fundamental conception, which, while complete and perfect for the asymmetric carbon atom, presented at the outset for unsaturated bodies a kind of doubt and difference of opinion, as we shall see. And, on the other hand, the experimental verification has much more serious obstacles to encounter in this case, and we have to recollect that only by the quite recent researches of

Wislicenus [1] has it become possible to advance a definite solution of the problem.

Entering a little into historical detail it is to be noticed in the original enunciation that Le Bel and I have considered the problem from a slightly different point of view; while Le Bel [2] preferred to wait for the result of further researches before deciding whether the four groups united to doubly linked carbons are or are not in the same plane, my point of view led me [3] to suppose that these four groups are in fact so situated. Some years later Le Bel [4], from the result of the researches of Kekulé and Anschütz, expressed himself as of the same opinion, so that, although travelling on different lines, our conceptions have reached the same point.

Relative position of the groups united to the doubly linked carbon atoms.—The application of the fundamental conception, namely that the four groups united to carbon occupy the angles of a tetrahedron, to the problem of double-linked carbon demands a precise notion concerning the nature of this linking. We consider that the relative position of the two combined tetrahedrons corresponds to that which we have supposed the case in the single linking, supposing always that two angles of each tetrahedron now play the same part as one in the preceding case; and further in view of the equality of the affinities of carbon now universally accepted, we must admit a perfect identity in the part played by each of the two angles of the tetrahedron in the act of combination.

[1] Abhandl. der kön. sächs. Ges. 1887. [2] p. 5.
[3] p. 11. [4] Bull. Soc. chim. xxxvii. 300.

In order to construct the grouping which results from these considerations we propose to find the relative position intermediate between those which denote the single linking when each pair of angles respectively is united. For this purpose let us suppose a compound $CR_1R_2r\ CR_3R_4r$, and let us represent it in two different ways, obtained by retaining the same position for the grouping CR_1R_2, but by attaching the groups r and CR_3R_4r in the two different fashions indicated by the Figures XI. *a* and *b*. To pass now to the unsaturated combination $CR_1R_2CR_3R_4$, it is necessary to remove the two groups r and to give to CR_3R_4 a position intermediate between those occupied by it in the two cases described, a position easily conceivable by uniting the two into one figure (Fig. XII.). We are thus led to the intermediate position represented by Fig. XIII., where the two groups R_3R_4 are situated in the same plane as R_1R_2, a plane in respect of which the two positions in Fig. XII. are symmetrical.

Graphic representation.—The state of things just described can be represented in an extremely simple fashion, retaining the ordinary notation $CR_1R_2CR_3R_4$, but giving real significance to the successive order in the groups R_1R_2 and R_3R_4.

Prediction of isomerism.—Besides the relative position of the four groups $R_1R_2R_3R_4$ which has been described, there is a second position which equally satisfies the conditions laid down, but is nevertheless not identical with the first; in short, the groups R_1R_2 may be situated in the same plane with R_3R_4, and united each to the same atom of carbon as before, but with this difference, that R_1 is opposite R_4, and R_2 opposite R_3, as shown by the symbol $CR_1R_2\ CR_4R_3$.

Consequently we are in a position to predict an

isomerism not accounted for by the old structural formulae, and it is clear that this isomerism is to be expected equally in all cases where the group R_1 is different from R_2, and R_3 from R_4, no matter whether there is equality or not between the groups attached to different carbon atoms, so that the case $CR_1R_2CR_1R_2$ involves the same prediction of isomerism.

II. Verification of the Fundamental Conception.

General character of the isomerism foreseen in the case of doubly-linked carbon atoms.—We propose first to discuss the nature of the isomerism in question, because we have to notice a marked difference between the new isomerism and that which results from the presence of the asymmetric carbon atom. In fact, according to the principles laid down, there is here neither dissymmetry nor enantiomorphism in the atomic structure. So that there is no question of rotatory power with contrary sign in the two cases, or of the particular hemihedral crystalline form which accompanies this optical property; these properties in fact, as we shall see, are absent. But if these distinctive traits are not present, there is yet a sufficiently profound difference to be looked for in the other properties of the two isomers. The complete identity shown in this respect by oppositely active bodies, which was in complete concordance with the presumable equality in all dimensions of their molecules, for this very reason will in this latter case be wanting, since we are entitled to assume on the one hand a difference in the general physical properties, in the melting point, the specific gravity, the crystalline form, the solubility, &c., and on the other hand a similar difference in their chemical properties, in their stability, heat of formation, &c.

This difference in all properties, though predicted from the theory, serves to a great extent to explain the obstacles which the theory, as applied to unsaturated bodies, had to encounter. In fact, the isomerism accompanying the presence of the asymmetric carbon atom baffled entirely all interpretation by the different structural formulae, and such an attempt as we made brought with it its own justification. In the present case, however, the state of things is different; the nature of the isomerism in question does not entirely exclude all attempt at interpretation by the old structural formulae. Of such attempts, too, there has been no lack; on the contrary, some chemists have been persistent supporters of such a method[1] until at last, now one and now another, after a profound study of the isomerism in question, has considered this position untenable[2]. Quite recently this avowal has found its expression in the term 'allo-isomerism,' which Michael[3] has introduced to denote the inexplicable isomerism which as a general rule accompanies the formula $CR_1R_2\,CR_3R_4$.

From this point, then, to the simple interpretation given by us, is only a step, rendered easy enough, if not necessary, by the work of Wislicenus which we have mentioned.

Inexplicable cases of isomerism accompanying the formula $CR_1R_2\,CR_3R_4$.—For the convenience of arrangement of the new proofs in favour of the new views, we shall mark with an asterisk (*) those conclusive isomer-

[1] Vide the work of Fittig and his pupils on the unsaturated acids; Erlenmeyer, Berl. Ber. xix. 1936; Anschütz, Ann. Chem. Pharm. ccxxxix. 164.

[2] Friedrich, Ann. Chem. Pharm. ccxix. 362; Beilstein, Berl. Ber. xvii. 2262; Michael, Berl. Ber. xix. 1378, 1381; xx. 550, &c.; Berl. Ber. xv. 16; Ann. Chem. Pharm. cxviii. 249.

[3] Loc. cit.

isms which were already contained in the original list. We shall add, as far as the extent of our space permits, the reasons which exclude the interpretation of the isomerism in question by a difference in the constitutional formula according to the old theory, and to avoid all partiality in this respect, we shall consider as much as possible the reasoning brought forward by others. We will now review the several instances according to different groups:

A. *Derivatives of unsaturated hydro-carbons. Isomeric diiodethylenes*, CHI CHI, obtained by Sabanejeff[1] by treating acetylene with iodine, which present a very notable difference in specific gravity in volatility, and in melting point.

Isomeric monochloropropylenes, $CH_3CH\,CHCl$, obtained by Wislicenus[2] by heating the aqueous solutions of the isomeric $a\beta$-dichlorbutyric acids.

Isomeric bromopseudobutylenes, $CH_3\,CBrCHCH_3$, obtained by Wislicenus[3].

Isomeric dibromides of crotonylene, $CH\,Br\,C\,Br\,CH_2\,CH_3$, obtained by the same chemist[4].

Isomeric dichlorides of tolane, $C_6H_5CCl\,CCl\,C_6H_5$, one obtained by Zinin[5] by treating tetrachloride of tolane with zinc, the other by Limpricht and Schwanert[6] by treating stilbene with pentachloride of phosphorus. Since then several different ways have been given for obtaining these two bodies[7].

Isomeric dibromides of tolane, $C_6H_5CBrCBrC_6H_5$, obtained by Limpricht and Schwanert[6] by treating tolane with bromine.

[1] Ann. Chem. Pharm. clxxviii. 109. [2] Berl. Ber. xx. 1008.
[3] Abhandl. der kön. sächs. Ges. 1887, 77. [4] Loc. cit.
[5] Berl. Ber. iv. 288. [6] Ib. iv. 379; xii. 1974.
[7] Ib. xii. 1971; xv. 898; xvii. 833, 1165; Ann. Chem. Pharm. ccxlviii. 20.

Isomeric orthodinitrostilbenes

$(C_6H_4NO_2)\,CH\,CH\,(C_6H_4NO_2)$ [1]

Possibly *apiol and isapiol*

$(C_9H_9O_4)\,CH\,CH\,CH_3$ [2],

and *isomeric anethols*

$(C_6H_4OCH_3)\,CH\,CH\,CH_3$ (Beilstein).

Perhaps we may also add *α- and β-hydropiperonic acids*

$(C_7H_5O_2)\,CH\,CH\,C_2H_4CO_2H$ [3].

B. *Monobasic unsaturated acids and their derivatives (acrylic series). Isomeric β-bromacrylic acids*, $CHBr\,CH\,CO_2H$. It is very probable that the two isomers possible in this case have been obtained one by reduction of tribromolactic acid, the other by treating propiolic acid with hydrobromic acid. It is, in fact, one of those cases classed by Michael [4] in his group of 'Alloisomers.'

Isomeric β-iodacrylic acids, $CHI\,CH\,CO_2H$. We mention these acids in connection with the preceding. Stolz [5] observed this 'physical isomerism' in the addition product of propiolic acid and hydriodic acid, a product which is transformed into its isomer by heating its solution in ligroin.

**Crotonic and isocrotonic acids*, $CH_3.CH.CH.CO_2H$. To the proofs, which in the infancy of our theory led to assigning the same constitution to these two compounds, has been added the discovery of vinyl acetic acid [6] $CH_2CH\,CH_2CO_2H$, which has been clearly shown to be different from isocrotonic acid, for which this latter constitutional formula had been proposed for want of a better.

[1] Berl. Ber. xxi. 2073. [2] Ib. 1621. [3] Ann. Chem. Pharm. ccxvi. 171. [4] Berl. Ber. xix. 1385. [5] Ib. xix. 542.

[6] Ib. xvi. 2592. As to another interpretation of the constitution of this acid, see Perkin, Journ. Chem. Soc. 1885, 810.

**β-chloro- and β-isochloro-crotonic acids*, CH_3CCl $CHCO_2H$. Since I have adopted the same constitution for the acids of Geuther, my opinion has been confirmed by the experiments of Friedrich[1], and accepted by Michael[2].

α-chloro- and α-isochloro-crotonic acids, $CH_3CH\,CCl$. CO_2H. These isomers have been obtained by Wislicenus[3] by treating with potash the chlorine addition products of isocrotonic and crotonic acids.

α- and β-bromo- and isobromo-crotonic acids. We have here exactly the same state of things as in the chloro-products. A short time ago Michael and Browne[4] announced that they had obtained two isomeric β-acids of the constitution $CH_3CBr\,CH\,CO_2H$; a little later[5] they added a third corresponding to the formula CH_3 $CH\,CBrCO_2H$; and quite recently an isomer of the same constitution was obtained by Langbein[6].

Isomeric β-thioethyl- and thiophenyl-crotonic acids. On treating β-chloro- and β-isochloro-crotonic acids with the sodium derivatives of ethyl and phenyl mercaptan, two pairs of isomers belonging to this category have been obtained[7].

Bromo- and isobromo-methacrylic acids, $CHBrC(CH_3)$ CO_2H. These two acids have been obtained by treating citra- and mesa-dibromopyro-tartaric acids respectively with potash[8].

Tiglic and angelic acids, $CH_3CH\,C(CH_3)CO_2H$. These compounds give on reduction the same acid, methyl-ethyl-acetic[9], and identical products on treatment with potash (namely, acetic and propionic acids)

[1] Ann. Chem. Pharm. ccxix. 362.
[2] Berl. Ber. xix. 384.
[3] Ib. xx. 1008.
[4] Ib. xix. 1384.
[5] Journ. f. pr. Chem. xxxv. 257.
[6] Ber. Berl. xx. 1010.
[7] Ib. xx. 1531.
[8] Ann. Chem. Pharm. ccvi. 16.
[9] Ib. ccviii. 249.

and with permanganate[1] (aldehyde and carbonic acid), and are transformed one into the other by heat. There is thus every reason to assign to both the constitutional formula given. The case is the same for higher homologues.

Hydrosorbic and iso-hydrosorbic acids[2], $CH_3CH:CH(C_3H_5O_2)$.

* *Hypogaeic and gaeidinic acids*, $CH_3.CH:CH.(C_{13}H_{25}O_2)$.

* *Oleic and elaidic acids*, $CH_3.CH:CH.(C_{15}H_{29}O_2)$.

* *Erucic and brassidic acids*, $CH_3.CH:CH(C_{19}H_{37}O_2)$.

B. *Monobasic unsaturated acids and derivatives* (*cinnamic series*). While the theory of constitution without the development which we are engaged in advocating admits of the existence of two *bromocinnamic acids* only, expressed respectively by the formulae $C_6H_5CBrCHCO_2H$ and $C_6H_5CHCBrCO_2H$, according to our conceptions there is room for four isomers, each of the above formulae in fact admitting of two different possibilities as to relative position. Now two isomers, obtained by Glaser, were at the time of the enunciation of the present theory already known, and the later researches of Erlenmeyer and Stockmeyer[3], and of Michael[4] have made known the other two missing bodies.

The isomer of *cinnamic acid* itself admitted by our theory appears also to have been obtained quite recently by Michael[5]; and we observe here that the *nitro-derivative of styrolene*, $C_6H_5CHCHNO_2$, corresponding in formula to cinnamic acid, and presenting also, according to us, a possibility of isomerism, is in fact transformed

[1] Berl. Ber. xvii. 2262.

[2] Ann. Chem. Pharm. cc. 51; ccviii. 67; Berl. Ber. xv. 618.

[3] Berl. Ber. xix. 1936.

[4] Ib. xix. 1378, 1381.

[5] Journ. f. pr. Chem. xxxv. 257. See also Liebermann, Ber. xxiii. 512.

into an isomeric product [1] which may be the body in question.

Among the chloro derivatives there are also grounds for believing that two *monochlorocinnamic acids* of the formula $C_6H_5CHCClCO_2H$ have been obtained [2].

Again, there are two isomeric *α-methyl cinnamic acids* $C_6H_5CH:C(CH_3)COOH$ [3].

The recently observed isomerism in the derivatives of *coumaric acid* $C_6H_4(OH).CH:CH.CO_2H$ is in all probability due to an analogous cause. We may notice as to this point that the alkaline salts of this acid, obtained by treating coumarin (the lactone of coumaric acid) by potash for example, undergo on heating an isomeric transformation into ortho-coumarates [4]; while the acid corresponding to these ortho-coumarates, produces in turn by treatment with hydrobromic acid the original coumaric acid and coumarin.

The *ethyl and methyl derivatives of coumaric acid* exhibit the same peculiarities [5]. On treating sodium coumarate $C_6H_4(ONa)CHCHCO_2Na$ with iodide of ethyl for example, a product is obtained isomeric with that resulting from the treatment of ethyl salicylic aldehyde $C_6H_4(OC_2H_5)COH$ with acetic anhydride, both corresponding in all probability to the formula $C_6H_4(OC_2H_5)CHCHCO_2H$.

C. *Dibasic unsaturated acids and derivatives.*

* *Fumaric and maleic acids.*—$CO_2H\,CH\,CH\,CO_2H$. The question of the isomerism of these acids has been

[1] Ann. Chem. Pharm. ccxxv. 340.

[2] Berl. Ber. xv. 1946.

[3] Ib. xx. 3396.

[4] Ann. Chem. Pharm. xlv. 334; lix. 183; ccxxvi. 351; Berl. Ber. xv. 2348.

[5] Journ. Chem. Soc. 1877, 414 and 418; 1881, 442; Ann. Chem. Pharm. ccxvi. 142; ccxxvi. 353.

treated so often that I think best to refer here to the recent expositions of Wislicenus[1] and of myself[2], with the anticipation that we shall consider later some of the points of view in question.

The halogen mono- and di-substituted derivatives of fumaric and maleic acids appear regularly to present all the peculiarities of the original compounds.

* *Citra- and mesa-conic acids* $CH_3 C CO_2H CH CO_2H$. The state of things here is the same as it was originally: we have the impossibility of interpreting the isomerism by a difference of constitution according to structure; an identical product of electrolysis $CH_3 CH CH_2$; an identical reduction product $CH_3 CHCO_2 H CH_2 CO_2H$; identical products of fusion with potash; possibility of mutual transformation; and we may add that the optical properties have led in both cases to the assumption of a double linking of carbon atoms[3].

There is also to be added to this series the lately observed isomerism in the case of *diphenyl fumaric* and *diphenyl maleic acids*[4].

We close this survey by observing that the series of isomerisms in question has been considerably enriched by quite recent researches, so that we have reason to expect that the proofs will shortly equal those which have brought about the almost general adoption of the conception of the asymmetric carbon atom.

Triple union of carbon atoms.—The case where the atoms of carbon are trebly linked, the case in short of the acetylene derivatives, only merits a passing glance from the new point of view, since it presents no differ-

[1] Abhandl. der kön. sächs. Ges. 1887, 27.
[2] Études de dyn. chim. 97.
[3] Berl. Ber. xiv. 2742; xvi. 3047.
[4] Ib.

ence from the old ideas. In the same way that we have constructed the grouping of the tetrahedrons in the double linking, we arrive at that which represents the case in question: the three angles of each of the tetrahedrons will be combined in an absolutely analogous manner, and consequently the two atoms of carbon with the two groups to which they are attached will lie in a straight line. There are no grounds for the prediction of any special isomerism.

Aromatic series.—With respect to the benzene derivatives the theory offers no new point of view unless it be that it accords a preference to the hexagon of Kekulé compared with the grouping in three dimensions of the six combined atoms, as for example in the prism formula. In fact, it is only in the first case that the groups introduced in the place of hydrogen in benzene, that is, the substituted benzenes, can give rise to no dissymmetry in the molecule, a dissymmetry which involves rotatory power; for instance, in the triangular prism formula the symmetry disappears on replacing two atoms of hydrogen situated diagonally, that is in the ortho-compounds. Now among the immense number of substituted derivatives of benzene found in nature (for example, salicylic aldehyde) there is not one which has exhibited rotatory power. Further, Le Bel[1] has in vain attempted the mesotomism of orthotoluidine, so that we are entitled to conclude the absence of dissymmetry in this case also.

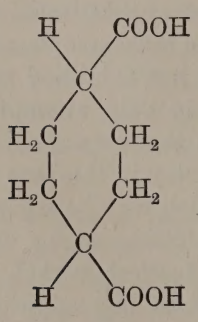
As to aromatic compounds which may be regarded as derived from the preceding by addition, as for example spirit of turpentine, camphor, borneol, carvol, quinic acid, &c., the theory gives without any addition, and based on the hexagon of Kekulé, as sufficient an explanation of the isomerism and of the activity as is met

[1] Bull. Soc. chim. xxxviii. 98.

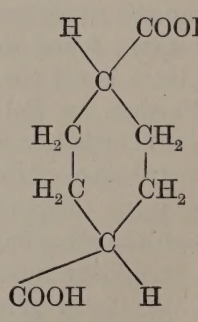
with in applying the principle of the asymmetric carbon atom in all its simplicity. For this reason these compounds have been included for our purpose among saturated bodies [1].

In the derivatives of pyridine we find the same conditions as in those of benzene, the absence of rotatory power; while the addition products in the former series, with conine, in short, with the active alkaloids, take their place alongside of the addition products of the aromatic series. To these also our theory applies without any supplementary considerations, and on this account they have been dealt with in the preceding chapters [2].

Classed with the aromatic compounds we may here refer to an isomerism among the derivatives of hexamethylene C_6H_{12}, an isomerism inexplicable by the old structural formulae, but an isomerism of which on the assumption of the tetrahedric grouping, we obtain a perfectly natural and obvious explanation. The most noticeable of these compounds is hexahydro-terephthalic acid [3], of which there are two isomers corresponding to maleic and fumaric acids, and represented by the formulae



I.



II.

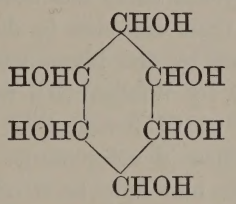
[1] See p. 29. [2] See p. 30.

[3] Baeyer, Ann. Chem. Pharm. ccxlv. 128.

The two carbon atoms, to which the carboxyl groups are attached, are in fact doubly linked, not directly, as in maleic and fumaric acids, but indirectly through the intervention of other groups.

This class of isomerism was alluded to in 'La Chimie dans l'Espace,' p. 41, in connection with the hydro- and isohydromellitic acids.

The same reasoning may be applied to account for isomerism among the glucoses, derived from hexamethylene, of the formula:



admitting of eight isomers.

Of these we have *Inosite*[1], and *Dambose*[2], which is probably identical with it, while *Scyllite* appears to be one of the isomers, and *Pheñose*[3] another.

Other instances of this isomerism among the hexamethylene derivatives may be mentioned:

Two benzene hexachlorides, $C_6H_6Cl_6$[4].

Hydro- and iso-hydromellitic acids, $C_6H_6(CO_2H)_6$[5].

α- and β-terpene tetrahydride, $C_{10}H_{20}$[6].

Among other bodies a similar explanation may account in part for the isomerisms of the terpenes and camphors.

[1] Compt. rend. civ. 225. [2] Ib. civ. 1853.
[3] Ann. cxxxvi. 323. [4] Compt. rend. xcviii. 436; Berl. Ber. xvii. 2256.
[5] Ann. Chem. Pharm. Suppl. vii. 43. [6] Beilstein, 2. Auf. 1, 152.

FIFTH PART.

FURTHER DEVELOPMENT OF THE THEORY.

During recent years there has been a manifest tendency from more than one side to develop further the original conceptions by the introduction of new consequences. A paper by Wislicenus[1], which has recently appeared, has led us to devote this chapter to a detailed account of these developments. In fact, while so far these new ideas had only been of service in the interpretation of known phenomena, they became, in the hands of that chemist, a means for the prediction of new facts which have already been corroborated by numerous observations.

There is the more reason for reuniting in a special chapter these recently acquired ideas, because they bring into prominence the chemical properties, such as the formation and transformation of geometrical isomers, while the original application only had regard to their physical properties and their number. The fundamental ideas, introduced for this purpose, may be collected into a twofold method of consideration, on the one hand having regard to the mechanism bringing about the addition in the case of the unsaturated organic compounds, and on the other hand having regard to the mutual action of the groups combined with the carbon.

[1] Abhandl. der kön. sächs. Ges. 1887.

I. Mechanism of addition in the case of unsaturated bodies.

General principle.—Before entering into details, we shall enunciate the principle on which are based the ideas to be developed concerning the mechanism of addition, a principle simple enough, being nothing else than that on which every conception of the mechanism of transformation of organic bodies is founded: namely, that the transformation takes place, leaving intact as much as possible the molecule undergoing such transformation.

Transformation of the triple linking into the double linking.—Since the two tetrahedrons, representing the triple union of carbon, are supposed to be joined by three pairs of angles respectively, and as in the double union two only of these pairs are still combined, the principle enunciated requires that in the transformation by addition there will only be destruction of the function of one pair of combined angles, the other two pairs remaining intact. It follows that a compound $R_1C.CR_2$ combining with R_3R_4 to form, for instance, $R_1R_3C.CR_2R_4$, will give rise to the formation of one of the two isomers possible, in this case that one which is represented by the symbol $C(R_1R_3).C(R_2R_4)$, where the groups R_1R_2 on the one side are supposed opposite to R_3 and R_4 on the other.

Let us quote as example a case which has been previously considered[1]: acetylene dicarboxylic acid $C(CO_2H)C(CO_2H)$ will produce in combining with hydrochloric acid the compound $C(CO_2H.Cl)C(CO_2H.H)$, corresponding, as we shall see, to chloromaleic acid, and not to its isomer $C(CO_2H.Cl)C(H.CO_2H)$.

[1] Van 't Hoff, Études de dyn. chim. 100.

Transformation of the double linking into the single linking.—In this case also absolutely analogous considerations apply, so that of the two pairs of angles represented as combined in the double linking, only one pair will be separated in the act of addition, the other pair remaining intact. We can trace the consequence of this in the following symbols, employing the method of projection described on p. 52. Let us suppose that the compound $CR_1R_2CR_3R_4$, or, what comes to the same thing, $CR_2R_1CR_4R_3$, combines with r_5r_6, in such a manner that r_5 is attached to the grouping $C(R_1R_2)$: the transformation will produce, taking into account the conditions described[1]:

$$\begin{array}{ccc} & r_5 & \\ R_1 & & R_2 \\ \hline R_3 & & R_4 \\ & r_6 & \end{array} \quad \text{or} \quad \begin{array}{ccc} & r_5 & \\ R_2 & & R_1 \\ \hline R_4 & & R_3 \\ & r_6 & \end{array}$$

that is to say, two different molecules $C(R_1r_5R_2)\,C(R_3R_4r_6)$ and $C(R_2r_5R_1)\,C(R_4R_3r_6)$ corresponding to compounds of opposite rotatory power. Now, since the two transformations have a perfectly equal chance of taking place, there will be the formation of an inactive mixture.

It still remains to facilitate the employment of our formulae in the case described. Let us observe that in this respect the two isomers can be written as follows, by a permissible transformation of the second notation, $C(R_1r_5R_2)\,C(R_3R_4r_6)$ and $C(R_1R_2r_5)\,C(R_3r_6R_4)$. Hence their derivation from $C(R_1R_2)\,C(R_3R_4)$ is simple: we have introduced the additional group between and after the groups R_1R_2 and R_3R_4, with this difference only, that at one time R_1R_2, and at the other time R_3R_4, have been separated by the interpolation. Again, selecting the

[1] See Fig. XI. *b* and XIII.

formula $C(R_2R_1)\,C(R_4R_3)$ identical with the former, we arrive at the following manner of combination $C(R_2R_1r_5)\,C(R_4r_6R_3)$ and $C(R_2r_5R_1)\,C(R_4R_3r_6)$, but this pair is identical with that previously obtained.

As an example a case may be given which has been previously considered [1]; namely, the combination of fumaric and maleic acids with hydroxyl to produce tartaric acid. The formula $C(H.CO_2H)\,C(CO_2H.H)$ corresponding, as we shall see, to fumaric acid, will give rise to the compounds $C(H.OH.CO_2H)\,C(CO_2H.H.OH)$ and $C(H.CO_2H.OH)\,C(CO_2H.OH.H)$, that is, to $C(H.OH.CO_2H)\,C(H.OH.CO_2H)$ and $C(H.CO_2H.OH)\,C(H.CO_2H.OH)$, that is, a mixture or combination of the two active tartaric acids, namely racemic acid. On the other hand, the other formula $C(H.CO_2H)\,C(H.CO_2H)$ leads to $C(H.OH.CO_2H)\,C(H.CO_2H.OH)$ and $C(H.CO_2H.OH)\,C(H.OH.CO_2H)$, that is to say, to two compounds identical and inactive by compensation, being nothing else than inactive amesotomic tartaric acid.

Inverse phenomenon. — If conversely a compound $C(R_1R_2R_3)\,C(R_4R_5R_6)$ is transformed into an unsaturated body, as by loss of the groups R_3 and R_6, the mechanism of action will again be the same, only in inverse sense. In the application, therefore, we must transform the formula in question so as to give to the groups to be removed the proper positions, namely, respectively between and after those groups which remain intact. We are thus led to the formulae $C(R_1R_2R_3)\;C(R_5R_6R_4)$ or $C(R_2R_3R_1)\,C(R_4R_5R_6)$, from which results $C(R_1R_2)\,C(R_5R_4)$ and, which is the same thing, $C(R_2R_1)\,C(R_4R_5)$.

We may mention here again a case which has been previously considered [2], namely the loss of hydrobro-

[1] Lagerung der Atome im Raume, p. 40.

[2] Études de dyn. chim. 100.

mic acid from isobromosuccinic acid $C(H.Br.CO_2H)$ $C(H.CO_2HBr)$, corresponding, as we shall see, to inactive tartaric acid. Transforming the formula we obtain $C(CO_2H.H.Br)$ $C(H.CO_2H.Br)$, giving $C(CO_2HBr)$ $C(H.CO_2H)$, which corresponds to bromofumaric acid.

Possibility of intramolecular transformations.—As is known, the reasoning relating to the mechanism of transformation in organic chemistry, based on the stability of the molecule, and hence requiring that the transformation which takes place will leave intact as much as possible the molecule which undergoes such transformation—this reasoning, I say, is not completely justified by experience without any exception. On the contrary, in more than one case of transformation the compound produced has not the constitution required by the principle in question, and this fact is justly attributed to an intramolecular transformation taking place during or immediately after the chemical action. It is not out of place to recall this fact here where the same principle finds a new application, and where there are grounds for expecting deviations from the principle of the same character, the more so as the mutual transformation of the geometrical isomers is brought about with remarkable ease. We may remark that the less elevated the temperature the more will these disturbing actions be eliminated, since experience has shown that heat is singularly favourable to intramolecular changes, without doubt owing to the acceleration it produces in the atomic movements.

II. Mutual action of the groups combined with carbon.

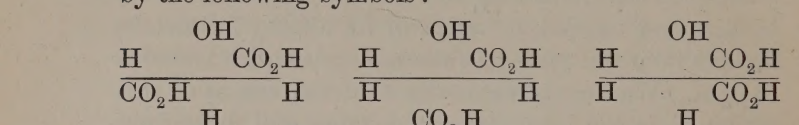
General principle.—We have grounds again for contention that the second consideration, introduced by

Wislicenus, is fully justified by its frequent application in other directions. In short, there can be no doubt, either from the theoretical or from the practical side, as to the reality of the influence which the different groups combined in a molecule exercise one on the other; as an instance we may cite the influence which in the carboxyl group is exercised by the oxygen doubly linked to the carbon on the hydroxyl in respect of its aptitude to exchange its hydrogen for a metal. That this influence will be closely connected with the chemical action of the group or of the atoms in question is probable if we only consider the smallness of the distance, limited as it is by the dimensions of the molecule; but it is also made sufficiently clear by the example chosen, where it is seen that oxygen, in virtue of its affinity for metals, favours their entrance into the molecule which contains oxygen. We may observe also that the extent of this action, as is the case with every force, will depend on the distance which separates the two groups, diminishing as this increases. Thus it is, still keeping to the same example, that oxygen in an organic molecule containing hydroxyl has not so striking an influence on this latter when the oxygen and the hydroxyl are not attached to the same carbon atom.

It is natural to wish to apply these principles in view of the precise notions introduced by our theory as to the distance between the different groups combined in an organic molecule. We propose to examine successively the different ideas which have been brought into prominence in this connection.

Prediction of the relative position of the six groups combined with two atoms of singly-linked carbon.—As a result of what has been stated, p. 51, the grouping representing a compound of the formula $C(R_1R_2R_3)$

$C(R_4R_5R_6)$ is only fixed in so far that the two atoms of carbon must each occupy one of the angles of the tetrahedron representing the relative positions of the groups combined with the other carbon atom. That being granted a rotation of one of the tetrahedrons about the axis which unites the two carbon atoms is still permissible, thus opening up the possibility of an unlimited series of different relative positions. Now Wislicenus observes that this position, being governed by the mutual action of the groups $R_1R_2R_3$ and $R_4R_5R_6$ on one another, can in a large number of cases be determined. To take an instance, Wislicenus has made choice among three of the different groupings conceivable for malic acid represented by the following symbols :



He accords his preference to the first of these formulae, where the negative groups OH, CO_2H are in as near proximity as possible to the positive atoms of hydrogen.

We can embody this idea in our simplified symbols, supposing the groups placed next the carbon to be opposite to one another.

The different positions given are then expressed thus—

$C(H.OHCO_2H)$, $C(CO_2H.H_2)$,
$C(H.OH.CO_2H)$, $C(H_2.CO_2H)$,
$C(H.OH.CO_2H)$, $C(H.CO_2H.H)$,

the first corresponding to malic acid. We may observe that in several cases, for example in the compound $HCCl_2.CHCl_2$, we should expect a position intermediate between the three illustrated.

We make the further addition, with Wislicenus, that

the atomic movements must introduce variations in the state of things described. In fact our whole theory, since it leaves such movements out of account, could only represent the reality as it would be at absolute zero. And looking at the matter from a practical point of view, in proportion as the temperature rises the state of things as regards malic acid will differ notably from that which we have adopted, and probably at a sufficiently high temperature all the relative positions of the groups $R_1R_2R_3$ with respect to $R_4R_5R_6$ will be found to be realised during sensibly equal intervals.

There remains to be added that, at the moment of the formation of an unsaturated body, the relative position of the six groups is determined according to the principle enunciated, p. 91, by reason of the necessary proximity of the two groups whose simultaneous action produces the transformation.

Relative stability of the two isomeric compounds, $C(R_1R_2)$, $C(R_3R_4)$ *and* (CR_1R_2), $C(R_4R_3)$.—As our theory explains the perfect equality in the stability of optically opposite isomers by reason of the absolute identity of all the dimensions conceivable in the two molecules, it ought also to apply itself to a marked difference in this respect among the unsaturated isomers, because it presupposes in this case a difference in the dimensions in question. In the above formulae, for instance, we suppose in one of the isomers that the two pairs of groups, R_1R_3 and R_2R_4, are brought into proximity, while in the other isomer, R_1R_4 and R_2R_3 are so situated. And in complete agreement with this notion we find that, while the transformation of active isomers is limited by the production of an inactive mixture in virtue of the equal stability of the two compounds, the transformation in the case of unsaturated isomers will be total. Now since

the nature of the groups $R_1R_2R_3R_4$ governs this stability, it is possible in certain cases at least to predict which of the two isomers will tend to be transformed into the other, always supposing the temperature be not too high, for here again heat will probably exercise a disturbing influence, opposed as it is to the clear expression of chemical affinity.

Keeping to the example of the fumaric and maleic acids corresponding to the formulae $C(HCO_2H)$, $C(CO_2HH)$ and $C(HCO_2H)$, $C(HCO_2H)$, we should expect a greater degree of stability attached to the former of these formulae where the negative carboxyl groups approximate as much as possible to the positive hydrogen atoms; and this greater degree of stability is in fact attached to fumaric acid.

Different aptitude of the isomers $C(R_1R_2)$, $C(R_3R_4)$ *and* $C(R_1R_2)$, $C(R_4R_3)$, *for special transformations.*— The supposed difference in the isomers in question is exhibited not only in their mutual transformations, but also in their reactions in a different direction. Thus we should expect in a transformation where the simultaneous action of the groups R_1 and R_3 comes in play, a greater aptitude in that isomer in which these groups are situated at the least distance, consequently in the compound $C(R_1R_2)$, $C(R_3R_4)$.

To quote an example, we have applied this principle[1] on the supposition that maleic acid, in virtue of the facility with which it loses water, contains the carboxyl groups, which both enter into this reaction, situated in closer proximity than they are in fumaric acid. This reasoning again leads to the formula $C(HCO_2H)$ $C(HCO_2H)$ for maleic acid.

[1] Die Lagerung der Atome im Raume, p. 40.

III. Applications and Verifications.

Transformation of unsaturated isomers facilitated by the presence of bodies capable of producing addition.— In commencing the account of a general property let us first instance the observation made in the case of maleic and fumaric acids, and afterwards show in every case of analogous isomerism, that the formation of the compound of greater stability is aided often in a striking manner by the presence of quantities, sometimes infinitesimally small, of bodies capable of producing addition. Thus, for example, I have observed that a trace of bromine, coupled with the action of the sun's rays, brings about the transformation of maleic into fumaric acid with such a completeness and readiness, that it has been possible to obtain well-defined photographs formed by a deposit of fumaric acid, in a thin layer of a saturated solution of maleic acid, in parts where this layer had been exposed for some seconds to light in presence of a trace of bromine vapour. In the same way iodine in minute quantity brings about the transformation of maleic ethers [1], while the acid behaves in an analogous manner [2]. The action, too, of nitrous acid on oleic acid, transforming it into elaidic acid, appears to be of the same nature.

These phenomena are in full accordance with the analogy in the mechanism, which we suppose to act on the one hand in the transformation, and on the other hand in the addition. We notice that this transformation amounts in fact to the rotation of one of the combined tetrahedrons about the axis joining the carbon atoms, to the effect that there is a separation of and then an exchange between the four united angles. In the addition we have also a separation of two united angles,

[1] Anschütz, Berl. Ber. xii. 2282.

[2] Kekulé, Ann. Chem. Pharm. Suppl. i. 134; ccxxiii. 186.

and this being equally possible on both sides of the molecule in virtue of its symmetry, we may consider it, in its first phase, that is before the addition product is formed, to bring about a change which results in the isomeric transformation in question.

Aptitude for addition in the case of the unsaturated isomer with inferior stability.—There is a second observation of a general nature to be added. Just as the analogy in the mechanism of isomeric transformation and of addition indicates the possibility of transformation being brought about by the presence of bodies capable of producing addition, in like manner this tendency to transformation will be favourable to saturation. This appears to be in all cases the general rule; thus, for example, comparing the rate of addition of bromine to fumaric and maleic acids in perfectly identical circumstances, namely in aqueous solutions of equal concentration, we find a greater velocity in the case of maleic acid [1], the less stable isomer.

Transformation of unsaturated isomers produced by the addition of bromine and removal of hydro-bromic acid.—We now have to deal with a third general property, this time of a much more striking nature, because we should never have expected it without recourse to the developments of the theory. The case appears a general one, but limiting it to one example let us recall the fact that maleic acid, after addition of bromine and removal of hydrobromic acid, is transformed not into the brominated derivative of maleic acid, but into bromofumaric acid. Similarly, starting from fumaric acid we obtain in this way the substitution product of its isomer [2].

[1] Études de dyn. chim. 103.

[2] Ann. Chem. Pharm. Suppl. ii. 92; cxxx. 1; cxcv. 6.

This transformation, of a sort that would seem in the future to offer a method of obtaining an immense number of unknown isomers predicted by our theory, is perfectly explicable by the light of the further developments of the theory. Considering, for the purpose of demonstration, the general case $C(R_1H)C(R_2R_3)$, we see that it is transformed not into its true substitution product $C(R_1Br)C(R_2R_3)$, but into the isomer $C(BrR_1)C(R_2R_3)$. The addition of bromine will in fact produce the bodies $C(R_1HBr)C(R_2BrR_3)$ and $C(R_1BrH)C(R_2R_3Br)$, or, which comes to the same thing, $C(BrR_1H)C(R_2BrR_3)$ and $C(BrHR_1)C(R_2R_3Br)$. Now on removing hydrobromic acid on the principle previously detailed, we arrive in both cases at the compound $C(BrR_1)C(R_2R_3)$.

It is thus that maleic acid produces directly by the treatment described bromo-fumaric acid and then dibromo-maleic; while fumaric acid yields directly bromomaleic and then dibromo-fumaric acid. The same is the case in the crotonic series, where the chlorine addition product gives rise on treatment with potash to chloroisocrotonic acid, while isocrotonic acid under the same circumstances furnishes chlorocrotonic acid [1].

Formation and transformation of Fumaric and Maleic acids.—The interpretation of the isomerism of these acids has been a favourite subject of study, since researches of this character are intimately associated with the progress of organic chemistry in general. The most diverse attempts at a solution of the problem have not been wanting. We may refer in a few words to these and to the success they met with as far as we can judge of it to-day. The interpretation which requires

[1] Wislicenus, Abhandl. der kön. sächs. Ges. 1887, 43, 44.

for fumaric acid a polymeric state has not been supported by the vapour density determinations of fumaric derivatives. We may observe that this hypothesis received its final form in the supposition of Anschütz[1], that the acid in question may be composed of two isomers with equal and opposite rotatory power, a supposition which he has abandoned[2] on account of the impossibility of mesotomism.

Again, the molecular weights of maleic and fumaric acids, as determined by Raoult's method, have been found to be identical[3].

The Kolbe-Fittig interpretation, which requires in maleic acid a divalent carbon atom, as indicated by the formula $CO_2HCH_2CCO_2H$, leads to the prediction of an analogous isomerism in the case of every derivative of ethylene, and even in the hydro-carbon itself. Now the list of thirty isomers, which at the present time belong to this category, and which all present the peculiarity of having the unsaturated carbon atoms combined with two different groups, renders the general conclusion, to which the interpretation in question leads, of but little probability. And we notice further that this hypothesis only explains the existence of the isomers without throwing any light on their properties.

The recent interpretation of Anschütz[4], which ascribes to maleic acid the formula

$$C(OH)_2CHCHCO,$$
$$|____O____|$$

appears to be confronted by an objection from the other side, since it confines to *acids* the isomerism in question, an isomerism which up to the present time has been observed in the case of six non-acid compounds at least.

[1] Berl. Ber. xviii. 1394. [2] Ann. Chem. Pharm. ccxxxix. 164.
[3] Comp. rend. cvi. 1735. [4] Loc. cit.

Further, such an isomerism, if this were its origin, should equally well find a place among saturated acids.

Finally we come to deal with Michael's hypothesis [1], a point of view which is unassailable because it offers not an explanation but an expression of the observed phenomena. According to this author, the case of the acids in question is one of an 'alloisomerism,' that is to say, an isomerism inexplicable by the ordinary formulae, and which constantly makes its appearance among unsaturated bodies if the doubly-linked carbon atoms are combined with different groups. We may express the hope that this impartial view will become assimilated to ours, when its author shall have considered the numerous verifications which our theory receives, not only as to the existence, but also as to the chemical properties of the isomers in question.

In fact, accepting for fumaric and maleic acids the formulae $C(H.CO_2H)$, $C(CO_2H.H)$ and $C(H.CO_2H)$ $C(H.CO_2H)$ respectively, and applying the principles detailed above, we find a host of peculiarities in the transformation and formation of these compounds which receive an easy and unlooked-for explanation.

1. *The greater stability of fumaric acid*, that is to say its ready formation from its isomer, is in full accordance with the supposed proximity of its negative groups (CO_2H) to its positive groups (H). That the halogen elements and their compounds with hydrogen, in short, bodies capable of producing addition, are favourable to this transformation, appears from the developments, on page 97. Further, the *greater aptitude for addition in maleic acid* being, according to these developments, in intimate relation with the inferior stability of this

[1] Berl. Ber. xix. 1378, 1381; xx. 530.

acid, our views receive support from this peculiarity also.

2. *The easy formation of maleic anhydride* in singular contrast to the impossibility of the analogous transformation of fumaric acid, is in full accordance with the proximity of the carboxyl groups in the former case. Further, the *extreme rapidity in the etherification of maleic acid*[1], resulting, as I have shown, from the preliminary formation of the anhydride[2], thus finds a perfectly natural interpretation if our conceptions are admitted.

3. *Formation of maleic acid from closed carbon chains* is again a curious peculiarity which is now explicable. We may observe that maleic acid is obtainable from benzene[3], by treatment with chlorous acid (producing trichlorophenomalic acid) followed by a treatment with potash; while on decomposing cinchomeronic and pyromucic acid maleic derivatives are again met with[4]. Now in these three cases we are dealing with a so-called closed carbon chain, where we have a grouping of atoms analogous to the grouping we suppose to exist in maleic acid, but different from that in its isomer.

4. *The exclusive production of fumaric acid on heating malic acid to moderately high temperatures* (150°)[5] is to be expected after what precedes. In fact, according to the principles laid down, the constitution of malic acid is expressed by the formula $C(CO_2H.OH.H)$ $C(H.CO_2HH)$, where the negative groups are supposed opposite to the positive groups. Now on eliminating water in the manner given on page 89, we obtain $C(CO_2HH)\,C(H.CO_2H)$, that is to say, fumaric acid.

[1] Menschutkin, Berl. Ber. xiv. 2630. [2] Études de dyn. chim. 104.
[3] Carius, Ann. Chem. Pharm. cxlix. 279; Kekulé, ib. ccxxiii. 170.
[4] Berl. Ber. xiii. 734, and Ann. Chem. Pharm. ccxxxiv. 86.
[5] Wislicenus, Abhandl. der kön. sächs. Ges. 1887, 28.

Further, directly we start from malic anhydride or the corresponding succinic anhydrides[1], thus introducing the approximation of the carboxyl groups as expressed by the formula $C(CO_2.OH.H)\ C(CO.H.H)$, we are led to the compound $C(CO_2.H)\ C(CO.H)$, that is, to maleic anhydride, which is in fact produced under these circumstances on superheating malic acid or on heating it in presence of acetyl chloride[2].

5. *We may mention again the unexpected transformation of maleic acid into bromofumaric and fumaric acid into bromomaleic*, on the removal of hydrobromic acid from the bromine addition products, a necessary change according to the developments on page 98.

6. We may add, as absolutely conforming to prediction, that *bromofumaric acid produces with hydrobromic acid isodibromosuccinic acid, which also results on treating maleic acid with bromine*[3]. In fact, bromofumaric acid $C(Br.CO_2H)\ C(CO_2H.H)$ in combining with hydrobromic acid will produce $C(Br.H.CO_2H)\ C(CO_2H.H.Br)$ and $C(Br.CO_2H.H)C(CO_2H.Br.H)$, which comes to the same thing as $C(CO_2H.Br.H)\ C(CO_2H.H.Br)$; but as we see, this acid will also result from maleic acid $C(CO_2H.H)C(CO_2H.H)$ by addition of bromine. Again, the production of dibromosuccinic acid isomeric with the preceding from both fumaric and bromomaleic acids by the action of bromine and hydrobromic acid respectively, is similarly explained[4].

7. *The formation of inactive tartaric and racemic acids by addition of hydroxyl to maleic and fumaric acids respectively* strikingly confirms our views. Maleic acid $C(CO_2H.H)C(CO_2H.H)$ must in fact produce under these circumstances $C(CO_2H.OH.H)C(CO_2H.H.OH)$

[1] Berl. Ber. xv. 643.
[2] Ib. xiv. 2791
[3] Ann. Chem. Pharm. cxcv. 67.
[4] Ib.

and $C(CO_2H.H.OH)C(CO_2H.OH.H)$, which are identical, and nothing else than inactive amesotomic tartaric acid. On the other hand, fumaric acid $C(CO_2H.H)C(H.CO_2H)$ would lead to the formation of $C(CO_2H.OH.H)C(H.CO_2H.OH)$ and $C(CO_2H.H.OH)C(H.OH.CO_2H)$, which amount to $C(CO_2H.OH.H)$, $C(CO_2H.OH.H)$ and $C(CO_2H.H.OH)C(CO_2H.H.OH)$, being nothing else than racemic acid. In full accordance with these predictions the oxidation of maleic and fumaric acids by permanganate in aqueous solution produces the compounds in question [1]. We may notice that dibromo- and isodibromo-succinic acids, corresponding to fumaric and maleic acids [2], are transformed under circumstances described by Anschütz [3], into inactive tartaric and racemic acids respectively. There is ground for supposing here an intramolecular change to have taken place, for which I think our theory could account.

8. There remains to be brought forward a confirmatory observation which we owe to Wislicenus [4]. This was the prediction that the addition of bromine to acetylene dicarboxylic acid $C(CO_2H)C(CO_2H)$ would produce $C(CO_2H.Br)C(CO_2H.Br)$, that is, dibromomaleic acid. Now Bandrowski had stated that dibromofumaric acid resulted from this reaction [5]. Guided by his advanced conceptions Wislicenus again took up the subject, and was in fact able to prove that dibromomaleic acid is the first product of this transformation; only he observed that if care is not taken to avoid the action of the hydrobromic acid formed by a secondary reaction, there is a further transformation to dibromofumaric acid which Bandrowski obtained.

[1] Berl. Ber. xiii. 2150; xiv. 713.
[2] Ib. xv. 1848.
[3] Ann. Chem. Pharm. ccxxvi. 191.
[4] Abhandl., &c. 37.
[5] Berl. Ber. xii. 2212.

In view of this rectification it does not appear premature to regard chloro-fumaric acid obtained on the one hand from tartaric acid by the action of pentachloride of phosphorus [1], and on the other hand by treating acetylene dicarboxylic acid with hydrochloric acid [2] as the isomeric secondary product of the transformation; in fact in both cases we have reason to expect chloromaleic acid.

Transformations observed in the case of other compounds.—Reviewing the other cases of isomerism belonging to the same category as fumaric and maleic acids, we find everywhere peculiarities at first sight curious, but which on reflection appear as natural consequences of the theory. Wislicenus has drawn our attention to this matter; and as instances we may mention the following:—

1. The difference of the chlorostilbenes, one obtained by the action of zinc on tetrachloride of tolane [3], the other by combining tolane with chlorine [4], might have been predicted; from what has previously been stated tetrachloride of tolane at the moment it loses chlorine corresponds to the formula $C(C_6H_5.Cl.Cl)C(Cl.C_6H_5.Cl)$ where the two atoms of chlorine to be removed are opposite, while the other chlorine atoms approach as near as possible to the phenyl groups: the action of zinc consequently leaves the compound $C(C_6H_5.Cl)C(Cl.C_6H_5)$. On the other hand, tolane $C(C_6H_5)C(C_6H_5)$ will by addition of chlorine produce the isomer $C(C_6H_5.Cl)C(C_6H_5.Cl)$.

2. *The different aptitude of the isomeric chlorocrotonic*

[1] Journ. f. pr. Chem. xxxi. 33.
[2] Berl. Ber. xv. 2694; Ann. Chem. Pharm. cxcv. 63.
[3] Berl. Ber. iv. 288.
[4] Ib. xvii. 1974.

acids $C(Cl.CH_3)C(CO_2H.H)$ *and* $C(CH_3.Cl)C(CO_2H.H)$ *for the removal of hydrochloric acid*[1] is perfectly explained by the proximity of the chlorine and the hydrogen in the second of these two cases. Now in complete accordance with this interpretation we find that that compound easily loses hydrochloric acid which results from the action of hydrochloric acid on tetrolic acid $C(CH_3)C(CO_2H)$[2]; in fact we have reason to expect in this case a compound corresponding to $C(CH_3.Cl)C(CO_2H.H)$.

3. In the case of *coumaric and ortho-coumaric acid* corresponding to the formulae $C(C_6H_4OH.H)C(CO_2H.H)$ and $C(C_6H_4OH.H)C(H.CO_2H)$ the special aptitude of one of the two to form coumarin, its anhydride, is in complete accordance with the proximity of the groups C_6H_4OH and CO_2H, which we represent in one of the above formulae. It is hence possible to predict that coumaric acid which, according to this supposition, contains the negative groups C_6H_4OH and CO_2H further from the positive H than its isomer, will also be less stable, in short will tend to be transformed into ortho-coumaric acid; the effect of heat on the coumarates shows us that the foreseen transformation takes place[3]. We may notice that there is here, both from the experimental and theoretical side, a marked analogy with the case of maleic and fumaric acids: there also the aptitude for dehydration accompanies inferior stability and according to us for absolutely analogous reasons.

The reasoning brought forward by Wislicenus in the pamphlet so frequently mentioned in this work has been subjected to much hostile criticism, especially at the

[1] Ann. Chem. Pharm. ccxix. 341–349. [2] Wislicenus, l. c. 43.
[3] Ann. Chem. Pharm. xlv. 534.

hands of A. Michael[1]. But it must be borne in mind that considerations of the nature of those brought forward by the German chemist cannot in their very nature be regarded as infallible in every case. There is, however, sufficient reasonableness in their application to most cases to render them of immense service in the development of the theory of chemistry in space. The fact that there is a closer resemblance between geometrically different than between structurally different isomers, and consequently a more ready transition in the former case from one isomer to another, may finally give sufficient reason for the obtaining one isomer in a reaction where at first we should expect to get the other.

Thus the attempts of Aronstein and Holleman[2] to obtain two isomeric stilbenes of the theoretically possible formulae $C(H.C_6H_5)C(H.C_6H_5)$ and $C(H.C_6H_5)C(C_6H_5.H)$ have apparently failed. It may be that the one stilbene known is more stable at ordinary temperature than its supposed isomer, and that the mere passing above or below a certain limit of temperature is sufficient to bring about a transition.

Such instances of molecular or isomeric change are not unknown. Thus ammonium nitrate, when heated above 78°, passes from the rhombic to the rhombohedral form, and the opposite change takes place on cooling[3]. A point of transition has been already noticed (p. 70) in the case of the tartrates and racemate of sodium and ammonium. Again, crystals of quinonedihydroparadicarboxylic ether, when alternately heated and cooled, keep changing from green to white and white to green[4].

[1] Journ. f. pr. Ch. xxxviii. 6.
[2] Berl. Ber. xxi. 2831.
[3] Lehmann, Molekularphysik, 1888, pp. 156, 158.
[4] Ib. 74, 176.

Hence it is not unnatural to expect a similar molecular transition in cases where it might not be so easy to detect it.

IV. Closed Carbon Chains.

It is now some years since V. Meyer [1], reviewing the general properties of carbon compounds, drew attention to the striking aptitude of this element for the production of closed chains of six atoms, as found in all aromatic bodies, and to the remarkable stability of such compounds, a fact the more striking in view of the difficulty of obtaining bodies containing closed chains of, for example, three carbon atoms, such bodies being then unknown. The same chemist insisted with reason on the presumption that more precise notions as to the structure of organic compounds should afford an explanation of such a fundamental property.

I took the opportunity to point out [2] that the new conception of the tetrahedric grouping was capable of explaining, to a certain degree at least, the peculiarity in question. These considerations, however, did not attract attention, and there would have been no reason to reproduce them here in their crude state, were it not that quite recently v. Baeyer [3], Wunderlich [4], and Wislicenus [5], each from his own special point of view, have developed absolutely analogous conceptions. There is, therefore, reason for reviewing them here. We shall not be dealing with a complete theory; but some remarkable properties will at least have some light thrown on them

[1] Ann. Chem. Pharm. clxxx. 192.
[2] Maandblad voor Natuurwetenschappen, vi. 150.
[3] Berl. Ber. xviii. 2278. [4] Config. organ. Molek. Würzburg, 1886.
[5] Abhandl. der kön. sächs. Ges. 1887, 57.

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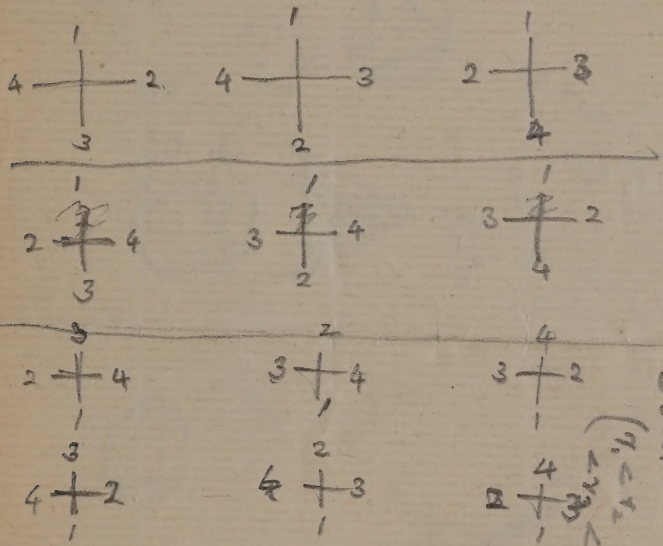
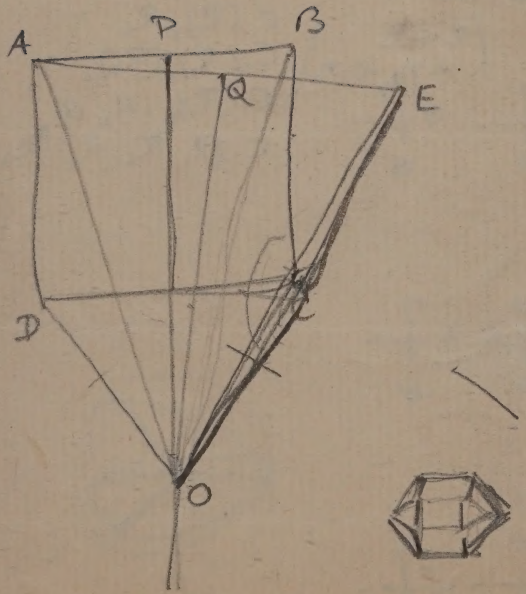
Outlines of Theoretical Chem. - L. Meyer (Longmans)



Models.

2 Regular Tetrahedra -
5 Tetrahedra. $C.(R_1)_4$
$C.(R_1)_3.R_2$
$C.(R_1)_2(R_2)_2$
$C.(R_1)_2.R_2.R_3$
$C.R_1.R_2.R_3.R_4$
$(\gamma_1 < \gamma_2 < \gamma_3 < \gamma_4)$



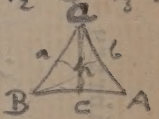
$C(R_1)_4$ —— $r_1 = r_2 = r_3 = r_4$

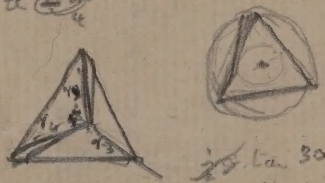
$C(R_1)_3 R_2$ —— $r_2 = r_3 = r_4 \neq r_1$

$C(R_1)_2 (R_2)_2$ —— $r_3 = r_4 \neq r_1 = r_2$

$C(R_1)_2 \cdot R_2 \cdot R_3$ —— $r_4 = r_1 \neq r_4 \neq r_3$

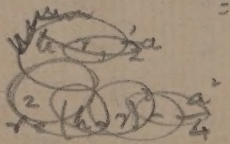
$C\ R_1 \cdot R_2 \cdot R_3 \cdot R_4$ —— $r_1 \neq r_2 \neq r_3 \neq r_4$





$h = \frac{1}{2}a\sqrt{3}$

$= \frac{1}{2} \cdot \frac{1}{3} \cdot \sqrt{3}$



$r = \frac{\sqrt{3}a}{6}$

$H = \sqrt{\frac{2}{3}a^2 - \frac{3a^2}{36}}$

$= \sqrt{\frac{12a^2}{36}}$

$= \sqrt{\frac{2}{3}} \cdot a$

which may be reflected back in a more complete and satisfactory manner.

The different observations which have given rise to the analogous considerations on the part of the chemists mentioned, present one feature in common, which we deal with first: the compounds, containing carbon in a chain of several combined atoms, are often capable of unexpected transformations, resulting preferably in the mutual action of groups widely separated. To take an example, we may notice that among the oxybutyric acids, it is just that compound in which the carboxyl and hydroxyl groups are apparently farthest apart, namely γ-oxybutyric acid $CO_2H.CH_2.CH_2.CH_2OH$, which readily forms a lactone, i.e. an anhydride resulting from the mutual action of the groups mentioned with loss of water. The observation is a general one: it is the γ-oxyacids having three atoms of carbon between the hydroxyl and the carboxyl which exhibit a special tendency to the formation of lactones.

Now our theory, so far from finding an obstacle in the mutual action of groups attached to carbon in a more complex chain, finds in it, if not an actual justification, at any rate an indication in that direction. We will now represent the grouping of several atoms of carbon combined according to our conceptions: the first atom C, will be situated as indicated by Fig. XIV. along with the two groups which it unites at the angle of an isosceles triangle C_1AC_2; A being 35° in virtue of the dimensions of the tetrahedron; the second atom of carbon C_2 will be situated together with the two groups C_1 and C_3, which it unites in its turn in an absolutely identical manner; it will be the same for a third C_3, a fourth C_4, and so on. Now it is clear that the distances AC_2, AC_3, separating the groups combined with the first atom, with the first

and second, with the first and third, &c., will not continue to increase. On the contrary, the ratio of these distances being represented by the ratio

sin 2A : sin 3A : sin 4A : sin 5A = 1 : 1.02 : .67 : .07,

a marked decrease will be introduced almost from the commencement, as the figure also shows.

After this general exposition we now enter into details. The simplest problem from the theoretical point of view is presented in the case of closed carbon chains: we have then to deal with only one element, and that one the relative positions of whose groupings are beginning to be unravelled.

Considering first the developments proposed by Baeyer[1] we must notice that this chemist, adopting in the closed chain polymethylenes a symmetrical grouping of the carbon atoms, compares the angle formed by the directions of the lines uniting two carbon atoms with a third, with the angle C_2C_1A of Fig. XIV. Now according as we are dealing with hexa-, penta-, tetra-, tri-, and dimethylene, the angle of the polyhedron in question comes to 120°, 106°, 90°, 60°, and 0° respectively, while the angle C_2C_1A of Fig. XIV. is about 109°; consequently the difference will be respectively 11°, 3°, 19°, 49°, and 109°, and in this difference the author finds an approximate expression of the tendency to saturation. In support of this reasoning we may mention the extreme difficulty of saturating hexa- and tetra-methylene derivatives, while trimethylene is capable of uniting with hydrobromic acid, but not with bromine, and dimethylene finally is saturated by the action of iodine.

The derivatives of benzene admit of an analogous application[2], fettered as it is by the difficulty of the

[1] Berl. Ber. xviii. 2278.

[2] Wunderlich, Config. org. Mol.; Van 't Hoff, Maandbl. voor Natuurw.

p.23. Why not 3 viz.:

$4 \overset{1}{\underset{3}{+}} 2 \quad 4 \overset{1}{\underset{2}{+}} 3 \quad 2 \overset{3}{\underset{4}{+}} 3$

p.25. Are the radii supposed to be equidistant (120°)?

problem, not yet definitely solved, of the manner in which the six atoms of carbon are combined. Accepting as a solution the notation of Kekulé where there is alternately a double and a single linking between the carbon atoms, let us compare with benzene the analogous closed chains admissible on the atomicity of carbon, viz. $(CH)_4$, $(CH)_4CH_2$, $(CH)_6$, $(CH)_6CH_2$ and $(CH)_8$.

For this purpose we give along with each formula the sum of the angles which our theory requires in the case of two carbon atoms combined with a third (about 109° in the case of a single linking; about 125° in the case of double linking between two of the three carbon atoms), and we give also the sum of the angles of the closed polyhedrons:

Formula.	Sum of Angles.	Angles of Polyhedron.	Difference.
$(CH)_4$	$4 \times 125 = 500°$	360°	140°
$(CH)_4CH_2$	$4 \times 125 + 109 = 609°$	540°	69°
$(CH)_6$	$6 \times 125 = 750°$	720°	30°
$(CH)_6CH_2$	$6 \times 125 + 109 = 859°$	900°	−41
$(CH)_8$	$8 \times 125 = 1000°$	1080°	−80

Hence we see that in benzene there is a maximum proximity, accounting for its stability and for the non-existence of the compounds mentioned along with it.

While the above observations refer only to carbon chains there are analogous remarks to be made concerning those to the formation of which different elements contribute; the stability of pyridine, thiophene, the γ-lactones, &c. would give grounds for analogous considerations, only they would have a less precise character, since the relative position of the groupings about elements other than carbon is absolutely unknown. Von Baeyer, too, confines himself to the con-

sideration of the bodies in question; Wislicenus[1], on the other hand, devotes to the subject a special consideration of extreme interest, which appears to open out for our theory a future not foreseen at its birth.

[1] Abhandl. der kön. sächs. Ges. 1887, 57.

CONCLUSION.

SINCE the French edition of this work was published, a very considerable amount of research has been done which bears directly on the problem of the position of the atoms in space. This theory and its consequences now form a special and important branch of chemical science, to which the name of 'Stereochemistry' has been applied. The work, published by Wislicenus in 1887, to which frequent reference has been already made in the preceding pages, marks an epoch in the history of chemical theory; and this chemist has recently been especially active in bringing forward new instances to support his views. Other chemists also have devoted special attention to this branch of chemical research, notably von Baeyer, Victor Meyer, Auwers, and Emil Fischer. Of these the former has dealt with isomerism among hexamethylene derivatives, Meyer and Auwers among the oximes, and Fischer among the glucoses. Besides these, we may mention the researches of Wallach on the terpenes, of Beckmann[1] on the menthols, of Bischoff and others on the substituted succinic acids, and of Lossen on the hydroxamic acids and their derivatives.

Much of the more recent work, as for example on the glucoses, has been embodied in the preceding chapters, but much still remains to be mentioned.

[1] Ann. Chem. Pharm. ccl. 322.

The Bromobutylenes, Tiglic and Angelic Acids.

The most striking of the recent work of Wislicenus is perhaps that in which is discussed the constitution of Tiglic and Angelic acids as dependent on that of the bromobutylenes[1]. In order to demonstrate clearly the bearing of the experimental results on the isomerism of these substances we must make use of the notation previously described (pp. 90–92); and the value of employing the notation in question will be evident from these examples.

The two bromobutylenes have the same structural formula:

$$CH_3, HC : C Br, CH_3,$$

and angelic and tiglic acids have also the same structural formula:

$$CH_3, H C : C CH_3, COOH.$$

Of the bromobutylenes, the one, which readily loses hydrogen bromide to give crotonylene, namely crotonylene hydrobromide, will have the formula $C(CH_3H)C(CH_3Br)$ since

$$C(CH_3)C(CH_3) + H Br = C(CH_3H)C(CH_3Br)$$

while the second, namely bromopseudobutylene, will have the formula $C(CH_3H)C(Br CH_3)$.

Angelic and tiglic acids unite with bromine to give the corresponding bromine addition compounds. These latter, by the well-known general reaction of β halogen acids, break up when treated with sodium carbonate in aqueous solution into hydrobromic acid, carbonic acid, and bromobutylene, the bromine atoms in the β position being in each case eliminated. From angelic acid is obtained in this way bromopseudobutylene, and from tiglic acid crotonylene hydrobromide.

Now the acid $C(CH_3H)C(CH_3COOH)$ on addition of bromine will give—

[1] Ann. Chem. Pharm. ccl. 224.

(*a*) $C(CH_3BrH)C(CH_3COOHBr)$ and (*b*) $C(CH_3HBr)C(CH_3BrCOOH)$; by transposing we get—

(*a*) $C(CH_3BrH)C(BrCH_3COOH)$ and $C(HCH_3Br)C(CH_3COOHBr)$.

(*b*) $C(HBrCH_3)C(CH_3BrCOOH)$ and $C(CH_3HBr)C(BrCOOHCH_3)$.

On now removing Br and COOH we obtain $C(CH_3H)C(BrCH_3)$, or which is the same thing $C(HCH_3)C(CH_3Br)$, that is to say, bromopseudobutylene. Hence the acid $C(CH_3H)C(CH_3COOH)$ is angelic acid.

In the same way it may be shown that the acid $C(CH_3H)C(COOHCH_3)$ yields $C(CH_3H)C(CH_3Br)$ viz. crotonylene hydrobromide, and is therefore tiglic acid.

Carbon atoms in a closed chain.

There appears to be some difference of opinion among chemists as to the stereometric isomerism conditioned by the groups attached to carbon atoms when these carbon atoms are situated in a closed chain. The matter is in reality quite simple. In the first place, with regard to asymmetry, of course no carbon atom situated in a closed chain can be combined with four different groups, but if it does not possess a plane of symmetry it will still be asymmetric. More simply we may say that, if the molecule has a nonsuperposable image, it will be asymmetric. It is not always easy to ascertain this from written formulae, but by constructing models of the molecule by means of tetrahedrons we are readily able to determine on which atoms the asymmetry of the compound depends.

Similarly, for other stereometric isomers, whether involving asymmetry of the molecule or not (see pages 86, 87); the models are invaluable for enabling us to ascertain the nature of the isomerism [1].

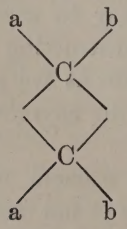
[1] Phil. Mag. 1888, p. 426.

Special isomerism in the case of the camphoric acids.

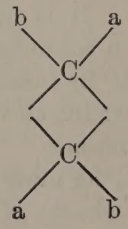
The camphoric acids afford the only instance at present known of an isomerism of the nature of that of maleic and fumaric acids associated with rotatory power. We know at present three camphoric acids, two laevo-rotatory and one dextro-rotatory. Of these one laevo acid is of the nature of fumaric acid, while the other two acids are maleoid; and the existence of a fourth acid, which will be dextro-rotatory and of fumaroid character, is already assured. There will further be two inactive acids obtained by mixing the two fumaroid and also the two maleoid acids together. The old meso-camphoric acid has been shown to be a mixture of the dextro-maleoid and laevo-fumaroid acids, and is not strictly comparable with substances inactive by mixture. It does not form a definite compound acid and is readily separated into its two constituents [1].

Nomenclature of stereometric isomers.

As to the adoption of distinctive names for stereometric isomers the use of the prefixes cis- and trans-, proposed by v. Baeyer, will be found convenient. This terminology is less cumbrous than the words maleoid and fumaroid, or axial and central symmetric. To give an instance we have:



cis-, maleoid,
axial symmetric.



trans-, fumaroid,
central symmetric.

[1] Comptes rend. cviii. 978; Proc. Roy. Soc. 47. 6.

For example, if we call the isomeric acids, obtained from malic acid by the action of heat, pyromalic acids, then maleic acid is cis-pyromalic and fumaric acid trans-pyromalic acid.

This nomenclature however will prove difficult in its application when the atoms or groups combined with one of the carbons differ from those attached to the other.

The Terpenes.

Wallach has subjected the terpenes to a complete and searching investigation, and a list of his papers is given below[1].

He has applied a new reaction, namely the action of bromine, to the identification and classification of the terpenes. He has, by means of this reaction and other older reactions, which he has modified and improved, been able to prove the identity of the chief constituents of many essential oils with other terpenes, and thus materially to diminish the number of definite isomeric bodies of this class.

It will not be possible here to do more than briefly allude to the present state of the chemistry of the terpenes. We have three principal groups.

(1) The turpentine group, b.p. 158°, which yields liquid tetrabromides.

(2) The camphene group, m.p. 50°, b.p. 160°, which yields no tetrabromides.

(3) The citrene group, b.p. 180°, which yields crystalline tetrabromides.

The first group includes terebenthene (−) and australene (+).

[1] Ann. Chem. Pharm. ccxxv. 291 and 314; ccxxvii. 277; ccxxx. 225; ccxxxviii. 78; ccxxxix. 1; ccxli. 315; ccxlv. 191, 241; ccxlvi. 221, 265; cclii. 94–157; ccliii. 249; cclviii. 319.

The second group includes + and − camphene, which may be obtained from the corresponding members of the first group in the following manner: the turpentine is acted upon by hydrogen chloride and the solid monohydrochloride thus formed gives, when hydrogen chloride is abstracted from it, not the original turpentine but camphene.

The third group includes + and − citrene, which occur in various essential oils, and inactive citrene (dipentene), which is obtained by mixing the two active compounds in equal proportions. Dipentene is also a constituent of many essential oils: it may also be obtained from turpentine by converting the latter into its dihydrochloride $C_{10}H_{16}\,2HCl$, which is identical with the hydrochloride obtained from dipentene and can be readily made to furnish this terpene.

The isomerism manifested in the terpene group, together with the peculiar nature of terpene derivatives, promises to afford material for a considerable extension of our views both as to structure and arrangement of the atoms in space. We are not however yet in possession of sufficient experimental material to discuss this matter in a satisfactory manner.

We are unacquainted, for example, with the precise nature of the isomerism in the case of the two members of the turpentine group, australene and terebenthene, nor do we know their relations to the inactive member of the group which Wallach has recently isolated, and which is distinct from the inactive mixture of the other two: this mixture, in fact, does not behave as if composed of optically opposite isomers. And as regards the camphene group, we are unable to account for the activity and inactivity of camphene according as it is produced in different ways, either from turpentine or

from borneol. We have again in the citrene and phellandrene groups a striking difference of properties. Whereas the inactive phellandrene closely resembles in properties its two active components, the inactive citrene has properties very different from its two constituents. In this case it may be that we have to deal with a particular *transition point* (see p. 72), above or below which we have a simple mixture or a compound as the case may be. A further point of interest in connection with the citrene group is that each member of it is capable of giving two distinct nitrosochlorides, and two classes of nitrolamines. We have here probably a case of the introduction into the formula of an additional asymmetric carbon atom. The formation of two classes of compounds would thus be analogous to the production of two borneols from camphor (p. 59), and two menthols from menthone.

Isomerism dependent on the Nitrogen Atom.

The remarkable success which has attended the stereochemical theory in its explanation of new facts has not unnaturally led to the application of analogous views of space-configuration to other elements than carbon, and more particularly to nitrogen. Without venturing to give any precise expression of opinion as to the mode in which the three or the five affinities of the nitrogen atoms are distributed in space, we may here recall the principal facts which bear on this question.

In the first place, we may call attention to the old controversy as to the equality or inequality of the five valencies of nitrogen, and to the work of V. Meyer and Lecco on the one hand, and of Ladenburg and Struve on the other. It would appear that triethyl-benzyl-ammonium iodide is capable of being obtained in

isomeric forms according to the order in which the hydrocarbon radicals are combined with the nitrogen[1]. These isomers may certainly be due to a difference in the value of the nitrogen affinities, but may equally be due, and this is, perhaps, the more natural assumption, to a different arrangement in space of the groups combined with the nitrogen.

But the chief interest attaching to the isomeric nitrogen compounds, qua nitrogen, centres in the derivatives of hydroxylamine. Lossen, from a study of the products of the action of anisyl and benzoyl chlorides successively on hydroxylamine, was led to suppose that all three atoms of hydrogen in the latter were of different value. He found that the successive replacement of hydrogen in hydroxylamine by the radicals benzoyl and anisyl, yielded a greater number of isomers than could be accounted for on the supposition that two of three hydrogen atoms in hydroxylamine were identical. Thus there are three compounds which may be represented as derived from hydroxylamine by the following formulae:

$$\text{I.}\quad N\begin{cases} OH_\alpha \\ H_\beta \\ H_\gamma \end{cases} \qquad N\begin{cases} OC_7H_5O \\ C_7H_5O \\ C_8H_7O_2 \end{cases}$$

$$\text{II.}\quad N\begin{cases} OC_8H_7O_2 \\ C_7H_5O \\ C_7H_5O \end{cases}$$

$$\text{III.}\quad N\begin{cases} OC_7H_5O \\ C_8H_7O_2 \\ C_7H_5O \end{cases}$$

More recently, however, Lossen[2] has come to the conclusion that the first action of an acid chloride on hydroxylamine is not a simple replacement of hydrogen, but an action comparable with that undergone by aldehydes with the same substance, and represented by the equation:

$$OHNH_2 + C_6H_5COCl = OHN : \underset{\displaystyle Cl}{\overset{\displaystyle |}{C}}.C_6H_5 + H_2O,$$

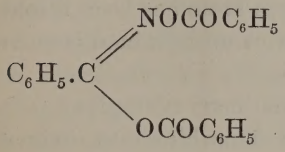
[1] Ber. x. 45, 309, 561, 964, 1152, 1634.

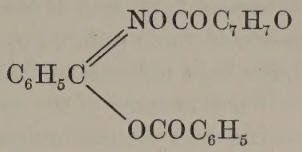
[2] Ann. Chem. Pharm. cclii. 170.

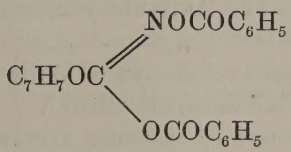
followed by a secondary reaction:

$$\begin{matrix} OH.N:C.C_6H_5 \\ | \\ Cl \end{matrix} + H_2O = \begin{matrix} OH.N:C.C_6H_5 \\ | \\ OH. \end{matrix} + HCl,$$

Thus he accounted for three trisubstituted derivatives by the further replacement of the other two hydrogen atoms either in the benzhydroxamic acid or in the anis-







hydroxamic acid. It is thus possible, without putting any great strain on the structural theory, to account for the three isomeric compounds. On the other hand, the former interpretation is the more natural, and may yet be found to be the true one.

But that is not all. If we accept Lossen's later views, there is still a case of isomerism, which he has discovered, and which is inexplicable by the structural theory. We are, in fact, acquainted with two different ethyl benzhydroxamic acids, which have the same structural formula $C_6H_5.C.OC_2H_5$, and which are both different

$$\begin{matrix} C_6H_5.C.OC_2H_5 \\ | \\ NOH \end{matrix}$$

from benzhydroxamic ether of the formula

$$\begin{matrix} C_6H_5.C.OH \\ | \\ NOC_2H_5. \end{matrix}$$

Another example of isomerism among hydroxylamine derivatives is that which has already been mentioned (page 58), namely, that subsisting in the case of the dioximes of benzile. Here, again, we have an isomerism inexplicable by the structural theory, and one which probably depends on the nature of the nitrogen atom.

Since the question of an isomerism conditioned by the space-configuration of the nitrogen atom has been raised, a considerable number of otherwise unexplained isomers have been referred to this cause.

We give some of the more prominent examples :

The two Benzaldoximes and Anisaldoximes, oximes of Benzaldehyde and Anisaldehyde respectively, investigated by Beckmann [1].

The dinitrohydrazobenzenes of Willgerodt [2].

Two acid oximidosuccinic ethers [3].

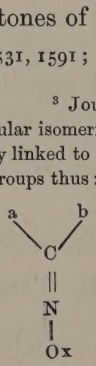
Numerous oximes of aromatic aldehydes and ketones yield two isomers analogous to the Benzaldoximes ; such are, besides those already mentioned, the oximes, or their derivatives, of Furfurol, Cuminol, Metanitrobenzaldehyde, Parachloro- and Parabromo- benzophenone, Paratolylphenylketone, Phenylthienylketone. This kind of isomerism has, however, not been observed in the case of the aldehydes, and ketones of the fatty series [4].

[1] Berl. Ber. xxii. 429, 516, 1531, 1591 ; xxiii. 1680 ; and Goldschmidt, ib. xxii. 3113 ; xxiii. 2163.

[2] J. Pr. Ch. xxxvii. 449.

[3] Journ. Chem. Soc. 1889, abs. 383.

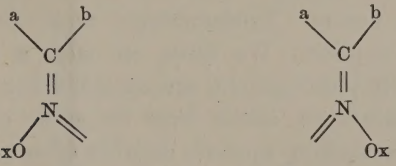
[4] We thus see that this particular isomerism has been found almost invariably when nitrogen is doubly linked to carbon, this carbon atom being united further to two different groups thus :



Movements of the atoms in the molecule.

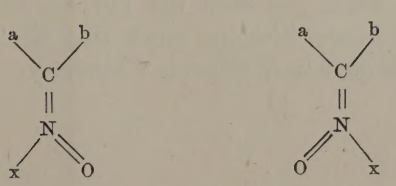
The original edition, 'La Chimie dans l'Espace,' began with the words 'Modern chemical theory has two weak points. It expresses itself neither as to the relative position of the atoms in the molecule nor as to their movement.' We have confined our attention in this work almost exclusively to the question of relative position. Incidentally, however, the movements of the atoms have also been considered. The very existence of asymmetry in respect of the carbon atom required that groups or atoms do not exchange places anyhow, a state of things which must inevitably result in the production of optical inactivity. But if the atoms or radicals change places at all, it must be in a regular

If we consider the nitrogen as pentad we get two different formulae :—



which may account for the isomerism. The two available affinities of the nitrogen atoms need not be regarded as really free but as serving to unite two molecules of the same kind loosely together, a state of things by no means improbable. (See Burch and Marsh, Journ. Chem. Soc. 1889, 656; Meldola and Streatfield, ib. 1890, 807; see also Hautzsch and Werner, Berl. Ber. xxiii. 11.) A similar explanation may be given, if we consider these compounds as derived from a hydroxylamine of the formula

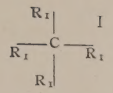
$$ON\begin{Bmatrix}H\\H\\H\end{Bmatrix}$$ thus :

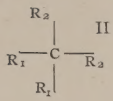


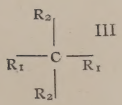
consecutive manner. Then again, the non-existence of an infinite number of isomers in the case of singly linked carbon atoms, required the possibility of a movement of rotation about their common axis, a movement which is excluded in the case of double linking.

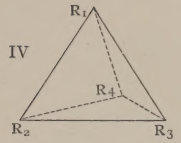
We have further the possibility of a change in atomic movement due to the action of heat and of solvents, and in the latter connection we may notice the change of rotation due to concentration, as in the case of malic acid dissolved in water. The electrolytic theory of solution may serve to explain this and analogous cases of change of rotation due to the action of solvents.

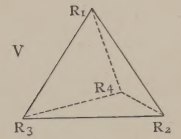
The question of intramolecular atomic movement has recently been considered from a new point of view, one, however, which may ultimately have some bearing on stereochemical theory. We refer to the phenomena to which the names 'Tautomerism' and 'Desmotropy' have been applied. We have, in fact, a number of instances, e.g. phloroglucin, acetoacetic ether, &c., where the same substance, either from its mode of synthesis or of transformation, appears capable of assuming more than one structural formula. Without dwelling on these cases at length, we may notice that here also an extension of the structural theory is necessary which shall take into account atomic movement. It may be that, when we have a better insight into the nature of these movements, an extension of the structural theory in this direction together with that extension, the demonstration of which has been the purpose of this book, will in the future illumine much that is now obscure in the whole domain of Organic Chemistry.

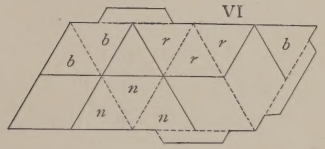


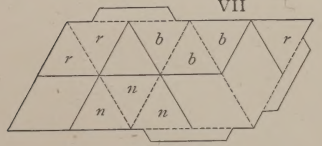


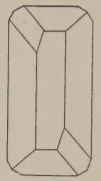


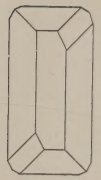


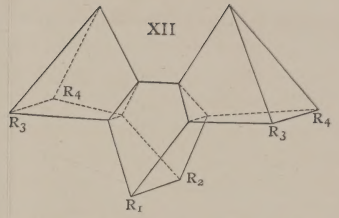


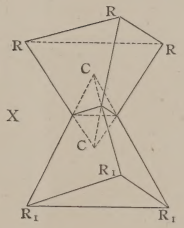


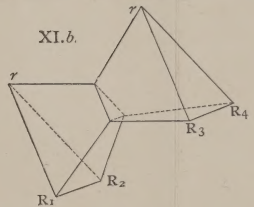


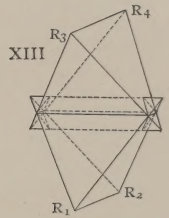


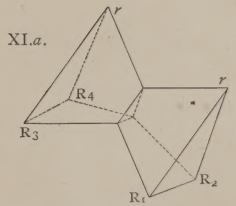


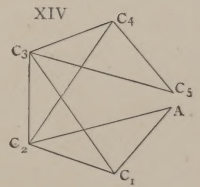












'CHEMISTRY IN SPACE.' — DIAGRAMS.

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